



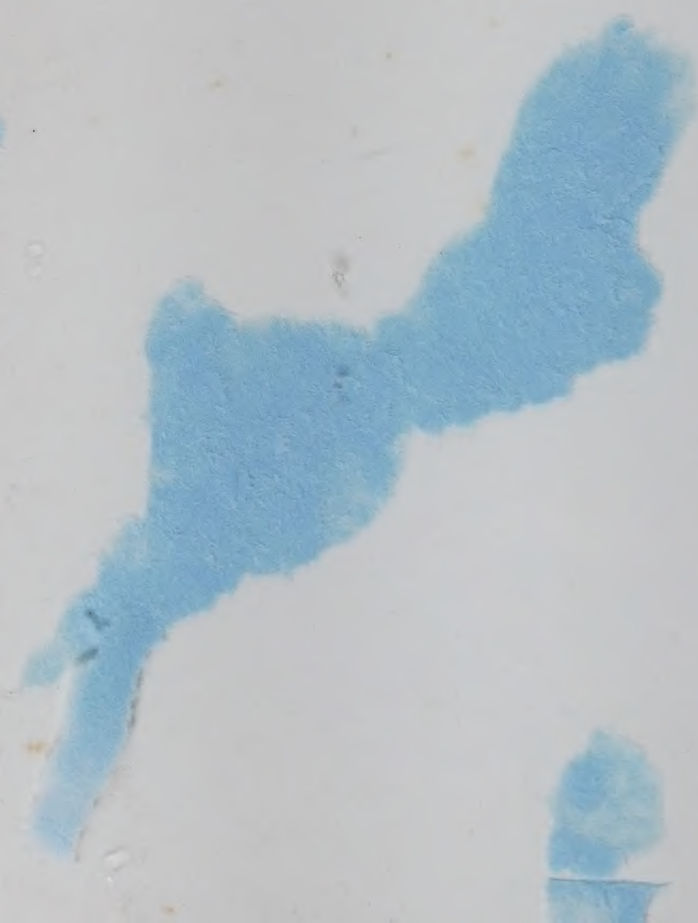
David R. Rudy
Kurt Kurowski

FAMILY MEDICINE



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Family Medicine

David R. Rudy, MD, MPH

*Pomerene Chair of Family Medicine
Professor of Preventive Medicine
The Ohio State University
Columbus, Ohio*

Kurt Kurowski, MD

*Predoctoral Director and
Assistant Professor of Family Medicine
The Chicago Medical School
North Chicago, Illinois*



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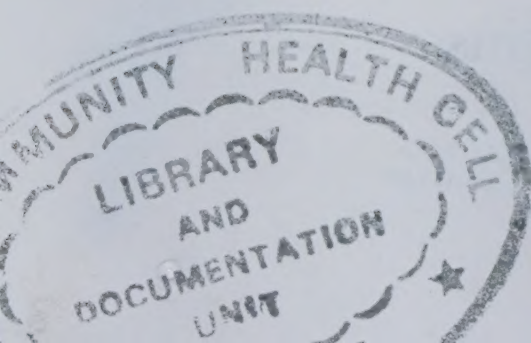
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We have undertaken this project enthusiastically in the belief that we could improve upon the practical works available for residents in their daily practices and pursuits. Our goal is to increase the convenience of practice by family practice residents, especially in the setting of the teaching family practice center, and to provide short reference material for didactic and preceptorial discussions. Most of this material is put out with the assumption that the reader, holding an MD degree and partly or completely trained in primary care, understands the basic sciences and the fundamentals of the subjects being treated; however, many bits of data, while once or often learned, require an availability of ready resources to reinforce or resurrect memory patterns called upon daily by family practice and internal medicine residents, as well as primary physicians in practice. In these regards, *Family Medicine for the House Officer* serves as a textbook and as a practice aid. A few chapters, such as some of those in the behavioral arena (i.e., 49, Counseling Models; 51, Anxiety, Phobias, and the Undifferentiated Primary Syndrome; and 52, Somatic Symptoms without Organic Basis), as well as some concepts laid out in the introductory chapter on prevention (36), pave entirely new territory for many in primary care. These can serve as more basic textual material for the student, the resident, and the attending physician.

We have further assumed that medical students and their professors can utilize this book in their third and fourth year family medicine clerkships and other primary care rotations. We feel the book applies not only as text material in their didactic sessions, but as a reference source in answering questions that arise daily in familiarizing the student with the problems of every day practice, both serious and benign.

David R. Rudy, MD, MPH
Kurt Kurowski, MD

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We wish also to acknowledge the clerical assistance of Peggy Pfeiffer-Norman of Chicago Medical School, Department of Family Medicine.

Finally, we appreciate our 57 contributors to 53 chapters, who represent academic family medicine and 16 other specialties in 21 universities and community hospitals from Hawaii to Washington, DC, and from upstate New York to Texas. They have provided us with immense intellectual stimulation and have widened our collegial horizons exponentially. We look forward to continued creative endeavors with them, including the day when we embark upon a second edition which will be thrust upon us soon enough by the inexorable proliferation of medical knowledge.

Contributors

James C. Anderson, MD

Pediatric Chief Resident
Baylor College of Medicine
Texas Children's Hospital
Houston, Texas

Glen F. Aukerman, MD

Professor and Chairman
Department of Family Medicine
The Ohio State University
Columbus, Ohio

Kay A. Bauman, MD, MPH

Associate Professor
Department of Family Practice and Community Health
John A. Burns School of Medicine
University of Hawaii
Honolulu, Hawaii

Daniel J. Bloch, MD, ABFP

Assistant Professor
Clinical Associate Residency Director
Department of Family Medicine
The Ohio State University
Columbus, Ohio

Edward T. Bope, MD

Family Practice Residency Director
Riverside Methodist Hospital
Clinical Associate Professor
Department of Family Medicine
The Ohio State University
Columbus, Ohio

Marjorie A. Bowman, MD, MPA

Professor and Chair

Family and Community Medicine

Bowman Gray School of Medicine

Wake Forest University

Winston-Salem, North Carolina

J. Timothy Bricker, MD

Associate Professor of Pediatrics

Baylor College of Medicine and Critical Care Medicine

Chief of Cardiology

Texas Children's Hospital

Chief of Pediatric Cardiology

Texas Heart Institute

Houston, Texas

Michael H. Bross, MD

Associate Professor

Department of Family Medicine

University of Mississippi Medical Center

Jackson, Mississippi

Cynthia M. Brown, MD

Associate Professor

Department of Family and Community Medicine

University of Nevada School of Medicine

Reno, Nevada

David R. Brown, MD

Assistant Professor

Department of Family Practice and Community Health

John A. Burns School of Medicine

University of Hawaii

Mililani, Hawaii

Anthony J. Cannistra, MD, MS

Director, Cardiac Catheterization Laboratory

Department of Cardiology

Memorial Hospital of Rhode Island

Pawtucket, Rhode Island

Assistant Professor of Medicine

Department of Cardiology

Brown University

Providence, Rhode Island

Mark E. Clasen, MD, PhD

Chair, Department of Family Medicine
Wright State University School of Medicine
Dayton, Ohio

Mary Thoesen Coleman, MD, PhD

Assistant Professor
Department of Family Medicine
The Ohio State University
Columbus, Ohio

Elise M. Coletta, MD

Assistant Professor of Family Medicine
Brown University School of Medicine
Providence, Rhode Island
Chief of Gerontology
Memorial Hospital of Rhode Island
Pawtucket, Rhode Island

Rob Crane, MD

Clinical Assistant Professor
Department of Family Medicine
The Ohio State University
Columbus, Ohio

Charles B. Eaton, MD, MS

Associate Professor
Department of Family Medicine
Memorial Hospital of Rhode Island
Pawtucket, Rhode Island

James M. Falko, MD

Professor of Internal Medicine
Division of Endocrinology, Metabolism, Diabetes
The Ohio State University
Columbus, Ohio

Jeanne M. Ferrante, MD

Assistant Professor
Department of Family Medicine
University of South Florida
Tampa, Florida

Eric P. Gall, MD, FACP, FACR

Professor and Chairman
Department of Medicine
Professor Microbiology and Immunology
Chicago Medical School
Chicago, Illinois

Bill G. Gegas, MD

Associate Program Director
Riverside Family Practice Residency
Riverside Methodist Hospital
Columbus, Ohio

Zvi Gross, MD

Senior Resident
Department of Family Medicine
The Ohio State University
Columbus, Ohio

Richard I. Haddy, MD

Professor
Department of Family Medicine
Wright State University School of Medicine
Dayton, Ohio

William G. Johnson, PhD

Professor and Director of Eating Disorders Program
Department of Psychiatry and Human Behavior
University of Mississippi Medical Center
Jackson, Mississippi

Mitchell S. King, MD

Director
Family Practice Residency
St. Francis Hospital of Evanston
Evanston, Illinois

Michael A. Krasnow, DO

Associate Professor
Department of Family and Community Health
Chief, Ophthalmology Section
Marshall University School of Medicine
Huntington, West Virginia

Kurt Kurowski, MD

Predoctoral Director and Assistant Professor
of Family Medicine
The Chicago Medical School
North Chicago, Illinois

Martin S. Lipsky, MD

Predoctoral Director
Department of Family Medicine
Medical College of Pennsylvania
Hahnemann University
Philadelphia, Pennsylvania

John A. Lombardo, MD

Medical Director, OSU Sports Medicine Center
Head Team Physician, OSU Athletic Department
Professor
Department of Family Medicine
The Ohio State University
Columbus, Ohio

Christopher G. Maropis, MD

Clinical Assistant Professor
Department of Family Medicine
Division of Sports Medicine
The Ohio State University
Columbus, Ohio

Karl E. Miller, MD

Associate Professor
Department of Family Medicine
University of Tennessee College of Medicine,
Chattanooga
Chattanooga, Tennessee

Amy Myers, MD

Clinical Assistant Professor
Department of Family Medicine
Division of Sports Medicine
The Ohio State University
Columbus, Ohio

Joseph J. Nidiry, MD, FACC

Associate Professor

Department of Family Practice and Gastroenterology

Howard University College of Medicine

Washington, DC

Sara L. Noble, PharmD

Assistant Professor

Department of Family Medicine and Clinical Pharmacy

University of Mississippi Medical Center

Jackson, Mississippi

Cynthia G. Olsen, MD

Associate Professor of Family Medicine

Executive Vice-Chair Department of Family
Medicine

Wright State University School of Medicine

Dayton, Ohio

Douglas M. Post, PhD

Assistant Professor

Department of Family Medicine

The Ohio State University

Columbus, Ohio

Gerald F. Ronning, MD

Assistant Professor

Department of Psychiatry

University of Illinois, Chicago

Chicago, Illinois

David R. Rudy, MD, MPH

Pomerene Chair of Family Medicine

Professor of Preventive Medicine

The Ohio State University

Columbus, Ohio

Linda Miller Savory, MD

Professor

Department of Family and Community Health

Marshall University School of Medicine

Huntington, West Virginia

Roger W. Schauer, MD, FAAFP

Director, Predoctoral Education in Family
Medicine

University of North Dakota

School of Medicine and Health Sciences

Grand Forks, North Dakota

Dara P. Schuster, MD

Assistant Professor

Internal Medicine

The Ohio State University

Columbus, Ohio

William A. Schwer, MD

Professor and Chairman

Department of Family Medicine

Rush-Presbyterian—St. Luke's Medical Center

Chicago, Illinois

R. Trent Sickles, MD

Associate Professor of Clinical Family Medicine

Department of Family Medicine

Division of Sports Medicine

The Ohio State University

Columbus, Ohio

Lori B. Siegel, MD, FACR

Assistant Professor of Medicine

Division of Rheumatology

Finch University of Health Sciences

The Chicago Medical School

Chicago, Illinois

Patrick O. Smith, PhD

Assistant Professor

Department of Family Medicine and Department of
Psychiatry & Human Behavior

University of Mississippi Medical Center

Jackson, Mississippi

Marna Sternbach, MD

Assistant Professor

Department of Family Medicine

Medical College of Pennsylvania

Hahnemann University

Philadelphia, Pennsylvania

Charles F. Streckfus, DDS, MA, FAOM

Associate Professor of Anatomy and Diagnostic Sciences

University of Mississippi Medical Center

School of Dentistry

Jackson, Mississippi

Steven W. Strode, MD, MEd

Associate Professor

Department of Family and Community Medicine

University of Arkansas for Medical Sciences

Little Rock, Arkansas

Gerald D. Suchomski, MD

Vice-Chairman

Department of Family and Community Medicine

Southern Illinois University

Springfield, Illinois

Vidya Sundaram, MD

Clinical Assistant Professor

Department of Internal Medicine

The Ohio State University

Columbus, Ohio

Marcia B. Szewczyk, MD

Assistant Professor

Department of Family and Community Medicine

Bowman Gray School of Medicine

Wake Forest University

Winston Salem, North Carolina

Jack E. Terry, MS, OD, PhD

Associate Professor of Pharmacology

Marshall University

Chief, Optometry Service

Coordinator, Research and Development

Department of Veterans Affairs Medical Center

Huntington, West Virginia

Donald J. Tosi, PhD

Professor Emeritus of Counseling Education
Department of Education
The Ohio State University
Columbus, Ohio

Ames F. Tryon, DDS, PhD

Professor
Department of Diagnostic Sciences
School of Dentistry
Associate Professor and Executive Director
Mississippi Geriatric Education Center
University of Mississippi Medical Center
Jackson, Mississippi

James B. Tucker, MD

Professor of Family Medicine
Residency Director, St. Joseph's Hospital
Department of Family Medicine
State University of New York Health Sciences Center
Syracuse, New York

Manuel Tzagournis, MD

Vice President for Health Sciences
Professor of Medicine
Department of Internal Medicine/
Endocrinology/Diabetes and Metabolism
The Ohio State University
Columbus, Ohio

Bruce T. Vanderhoff, MD

Associate Director
Grant Family Practice Residency
Grant/Riverside Methodist Hospitals
Assistant Clinical Professor
Department of Family Medicine
The Ohio State University
Columbus, Ohio

Michael B. Weinstock, MD

Clinical Assistant Professor
The Ohio State University
Columbus, Ohio

Mary Jo Welker, MD, FAAFP

Vice-Chair for Clinical Services
Department of Family Medicine
The Ohio State University
Columbus, Ohio

Russell Wenacur, MD

Resident Physician
Department of Family Medicine
St. Joseph's Hospital Health Center
Syracuse, New York

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Problems of the Head, Eyes, Ears, Nose, and Throat

Chapter 1

Problems of the Ears, Nose, and Throat

David R. Rudy

Upper respiratory chief complaints, excluding sore throat and ear pain, comprise 2.5% of outpatient complaints. They rank second and constitute 7.9% of diagnostic clusters in outpatient family practice. These complaints result in an approximate average of 8 to 15 visits per week, varying greatly with the season of the year (1, 2).

CORYZA AND RHINITIS

The word *coryza* is convenient to describe the constellation of aqueous discharge from nose and eyes plus sneezing and a degree of scratchy sore throat common to many conditions.

Uncomplicated Viral URI (The Common Cold)

They occur at all ages, and are caused by a large variety of viruses, including rhinoviruses (most common), enteroviruses, para-influenza, influenza A and B and respiratory syncytial viruses (RSVs). RSVs have the highest complication rate.

In adults, the course of an uncomplicated cold is generally 10 days with more or less three stages. A prodrome, lasting 1 to 3 days, consists of a scratchy sore throat, plus drowsiness and mild chilliness. The throat soreness tends to be worse in the mornings, whereas streptococcal pharyngitis pain tends to be worse toward the evening. Physical findings are limited to palatal venulectasia superimposed on a pale, slightly edematous background, contrasting with classic strep pharyngitis, which, if exhibiting erythema, shows a diffuse redness. Symptomatic treatment at this stage consists of benzocaine lozenges, such as Cepostat.

The coryzal phase begins on the second to fourth day. Cough may be present but is mild and emanates from a tracheal level and may interfere with sleep. The symptoms of coryza respond to the classic blocking antihistamines but only for about 3 days, shortening neither the contagious nor symptomatic periods.

In the third phase, the nasal discharge thickens. The cough may require suppression at night with codeine or related medication. Later, the cough becomes more productive, of whitish sputum, and emanates from the large bronchi. An expectorant without a narcotic is the best cough preparation in the productive stage. In nonsmoking non-atopic individuals, the cold resolves as this phase ends, on the 10th to 14th day.

Complications usually occur during the second and third phase and include otitis media (sporadically in normal children or recurrently in those with atopic disease or other eustachian tube dysfunction, less likely in adults); sinusitis; bronchitis with or without bronchospasm; pneumonia, and reactive airway disease (Chapter 11). The latter is notably more likely in atopic individuals and in smoking adults.

Allergic Rhinitis

This is the main component of the syndrome of hay fever, a disease of nasal and other upper respiratory IGE-mediated reactivity to airborne antigens. It occurs virtually always in people who have other atopic diseases (history of infantile eczema, asthma, atopic dermatitis) and/or family history of such problems. The

other components of hay fever are scratchy, itching sore throat, allergic shiners, and itching conjunctivitis. Treatment is any of a number of H₁ blockers (Chapter 35). Symptoms may briefly be confused with the first phase of a cold.

Vasomotor Rhinitis

In its pure form it is a condition of boggiess of the nasal mucosa associated with a complaint of stuffiness. Typically, the mucosal congestion is labile, the stuffiness setting on rapidly and often remitting just as quickly. It is a psychophysiologic disorder, some believe an expression of suppressed weeping, often unacknowledged depression. Many patients resort to proprietary topical decongestants and soon compound the problem with development of *rhinitis medicamentosa*. They may respond well to inhaled glucocorticoids as aids for tolerable withdrawal from the nasal decongestants. These patients, however, may be amenable to psychotherapy, an approach more directed to cause.

Rhinitis Medicamentosa

Patients with this disorder are virtually diagnosable by sight and sound, because of their severely obstructed nasal airways. Speech is hyponasal, and breathing is oral. The cause is overzealous use of proprietary nasal decongestants, all of which induce local tolerance resulting in progressively shortened drug effect and rebound boggiess. The advent of inhaled nasal glucocorticoids has made rapid withdrawal from the medication much easier. Short-term systemic glucocorticoids are successful also. Otherwise the treatment consists of taking the patient off the nasal decongestant drops quickly without medication support. The patient suffers through the first waking day. A clean warm wet cloth is placed across the nose and mouth at onset of sleep. The first night of withdrawal will be the most difficult.

Epistaxis

Anterior Epistaxis

Most occur in the anterior septal region, consisting of venous bleeding, usually from digital trauma, mucosal drying or congestion secondary to viral upper respiratory infection or allergic rhinitis. Individual episodes last less than 10 minutes except in the face of coagulation disorders, whether inherited, due to blood dyscra-

sia or aspirin intake. Recurrences may take place for varying periods, over hours or days. A history of bleeding from only one side confirms an anterior location. The patient may be coached by phone to control by tamponade the affected side, pressing the soft tissue of the naris for 5 to 10 minutes medially against the septum. A cotton pledget soaked with phenylephrine (Neo-Synephrine) or oxymetazoline (Afrin) may be held against the site of bleeding. If these fail, the bleeding site must be identified, and silver nitrate cauterization of the venous bleeding site can be accomplished, usually after application of 4% lidocaine for local anesthesia. Bleeding diathesis should be considered as treatment is effected, checking prothrombin, partial thromboplastin, and bleeding times.

Posterior Epistaxis

This is usually from arterial bleeding, often requiring otolaryngologic consultation. They tend to occur in hypertensive individuals or the elderly. Posterior catheter balloons, packs or tampons may be placed by any physician comfortable with the procedure. The patient may be sedated with meperidine (Demerol) 50 to 100 mg intermuscularly (IM) beforehand, blood pressure permitting.

PROBLEMS OF THE EAR

Otitis Media

Purulent otitis media is seen in children in daily practice, regardless of the time of the year. Especial susceptibility is found in American Indians, Eskimos, boys > girls, children with Down syndrome and with cleft palate. In the absence of underlying pathology, it is normally sporadic between the ages of 4 to 5 months and 2 years (Table 1.1). Adult cases occur sporadically into middle age.

The pathophysiology involves underlying poor drainage from the eustachian tubes, because of congenital deformity, especially with cleft palate; adenoidal hypertrophy; edema and congestion from current viral URI, or allergy in atopic individuals (ages 2 to 10 or older). Atopic disease and adenoidal hypertrophy underlie a great proportion of persistent and recurrent otitis media. Adenoidal hypertrophy tends to occur in atopic individuals as well, and may respond to inhaled glucocorticoids, effecting medical adenoidectomy. Seventy-eight percent of recurrent otitis media has been associated with food (and presumably atopic) allergies of whom 86% will respond to appropriate dietary management

Table 1.1.
Otitis media.

Cumulative Incidences	Epidemiology and Susceptibility:	
	Acute, Once	Recurrent (≥6 Bouts)
Through age 1	60%	1–2%
Through age 3	80%	20%
Through age 5	90%	30%
Through age 7	90%	40%

Reprinted with permission from Teele DW, Klein JO, Rosner B. Epidemiology of otitis media during the first seven years of life in children in greater Boston: a perspective, cohort study. J Infectious Dis 1989;160(1):83.

(with an unknown proportion responding to atopic desensitization and other management) (3). The appearance of the drum varies from annular erythema to angry redness to bulging red or pus colored.

Viral upper respiratory disease precedes sporadic otitis media in the vast majority of cases. Respiratory syncytial virus infection results in a 1:3 risk, while the common cold virus (rhinovirus) only 10% (Table 1.2). The much greater incidence of cold viruses accounts for the greater overall association with colds.

The pain of otitis media is caused by tension on the tympanic membrane; traction in *secretory otitis media* and pulsion if/when the process becomes exudative. In the former, the drum is drawn inward over the ossicles, like cellophane, with relatively clear fluid level or globules behind the drum.

Secretory Otitis Media (Middle Ear Effusion)

In *aerotitis* or *barotitis media*, the pressure differential develops rapidly at the time of descent in an aircraft, usually coincident with upper respiratory congestion. There may be intense pain and hemorrhage. The retracted eardrum shows hemorrhage along with fluid locules or levels. The middle ear is sterile. Fifty percent of cases resolve within 8 weeks.

Purulent Otitis Media

It is a bacterial infection in 70% to 90% of cases, complicating the described conditions of congestion. The organisms involved in descending frequency are: *Streptococcus pneumoniae*, *Hemophilus*

Table 1.2.
Risk of otitis media after acquisition of virus.

	% with AOM after 2 weeks
RSV	33%
Adenoviruses	28%
Influenza, A and B	28%
Para-influenza	16%
Enteroviruses	15%
Rhinoviruses	10%
No viruses	7%

Reprinted with permission from The New England Journal of Medicine, Massachusetts Medical Society. Henderson FW, Collier AM, Sanyal MA, et al. A longitudinal study of respiratory viruses and bacteria in the etiology of acute otitis media with effusion. *N Engl J Med* 1982;306(23):1379.

influenza, *Maroxella catarrhalis*, beta hemolytic *Streptococcus pyogenes*, *Staphylococcus aureus*, and others with different authors reporting variably. Table 1.3 shows representative data. The remainder show negative cultures, most of which are presumed to be solely of virus etiology. One third of *H. influenza* are highly lactamase producing, and 80% to 90% of *M. catarrhalis* are low-grade producers. Thus, resistance to amoxicillin is a factor in about one-fourth of cases.

While fever and pain are inconstant and inconsistent, hearing loss is not. Conductive hearing loss and an immobile eardrum are necessary to diagnose otitis media. Conductive hearing loss is diagnosed by tuning fork tests (Weber, Rinne). Adults with middle ear infection often come to the doctor more because of the stuffy sensation in the ears than for pain. Hearing loss may be noticed by the school nurse, teacher or parent due to chronic secretory otitis media. Overdiagnosis occurs from relying on color change of the drum without confirmation of conductive hearing loss. Air insufflation through a closed headed otoscope with a soft gasketed speculum reveals the drum to be immobile.

The patient's temperature may be normal even during acute and severe earache (in as many as 75%) but often is as high as 102°F (39°C). The ear is devoid of external tenderness unless otitis externa coexists.

Before the advent of antibiotics, though the great majority recovered without sequelae, otitis media was fraught with complications ranging from erosion into the mastoid air cells, to meningitis and death. First-line antibiotic treatment consists of amoxicillin 20

Table 1.3.
Bacteria involved in purulent otitis media.

Strep. pneumonia	46%
(0–60% pcn resistant, nonlactamase)	
H. influenza	19%
(⅓ resistant, lactamase, “high grade”)	
M. catarrhalis	22%
(80–90% resistant, lactamase, “low grade”)	
Str. pyogenes	4%
Other	5%
“Sterile”	4%

Hence, about 25% will resist amoxicillin.

Reprinted with permission from DelBoccaro MA, Mendelman PM, Inglis AF, et al. Bacteriology of acute otitis media: a new perspective. J Pediatr 1992;120(1):81–84.

to 40 mg/kg in divided doses three times per day for 10 days. The adult dosage is 250 mg every 8 hours. If lactamase production is suspected or if the otitis is recurrent or persistent, amoxicillin/clavulanic acid (Augmentin), or trimethoprim/sulfamethoxazole (TMP/SMX [Bactrim, Septra]) or ampicillin/sulbactam (Unasyn, intravenous only) are used. If penicillin allergy is present, erythromycin (with sulfisoxazole for hemophilus) or clarithromycin is indicated. *Resolution* may occur within 48 hours to 3 weeks and is defined as freedom from pain without hearing loss. Seventy-five percent of cases will resolve within 10 days (4); 90% within 3 months, of whom only 10% will resolve spontaneously. Most physicians prefer the first re-examination of the ear in approximately 1 week. Failure of the patient to follow up occurs in 22%, some of which may be related to sound parental judgment of success (5).

Outcomes and Their Management in Otitis Media. *Unresponsiveness*, i.e., pain continuing after 48 hours, occurs in 10% and is approached by repeat or change of antibiotic, with attention to lactamase production. Resistance of Streptococcus pneumoniae to penicillin and other antibiotics varies from 10% in some regions of the United States to more than 50% in others.

Residual effusion, for up to 16 weeks, is within the realm of acceptable outcomes.

Persistent effusion (beyond 16 weeks) associated with a 20 db hearing loss by definition; also called persistent otitis media, occurs most likely in association with the risk factors mentioned previously (6). Fifty percent to sixty percent occur in atopic individuals. It may be managed by repeat or change in antibiotic for 10- to 14-day

courses in combination with short-term glucocorticoids. Inhaled glucocorticoids may be effective in reducing eustachian tube congestion and adenoidal hypertrophy. Persistence beyond 4 months after two additional courses of antibiotics is an indication for ventilation tubes.

Recurrent otitis media (ROM), defined as ≥ 4 attacks within a year or ≥ 3 within 6 months, occurs in 10% to 15% of cases, is managed by repeated and alternative antibiotics as outlined. Influenza and pneumococcal vaccinations are given at the same time. If repeated antibiotic courses fail, antibiotic prophylaxis is prescribed throughout the course of the upper respiratory infection and carried throughout the winter months. This will reduce the frequency of recurrences by nearly half (5). Failing this, inhaled steroids should be tried as long as no recurrences are seen. Finally, tympanostomy tube placement reduces frequency of recurrence in an additional 50% for a 2-year period.

Ultimate medical failures are managed with myringotomy, tympanostomy, adenoidectomy alone and combined tympanostomy/adenoidectomy (6).

Management of Tympanostomy Tubes. These are effective in immediate relief of effusion and remediation of hearing loss, and are normally extruded in most cases within 6 to 24 months. Some have remained indefinitely. If tubes have to be replaced within 2 years, adenoidectomy may be effective in many cases. Tonsillectomy and adenoidectomy are done far less often than in the past, and indications are partial airway obstruction (snoring, chronic mouth breathing) rather than recurrent otitis media and hearing loss.

Chronic Otitis Media

This nearly always presents as a perforated eardrum, not visualized when the external canal is filled with exudate or other debris. Often the anatomy is grossly distorted due to the presence of a cholesteatoma. Though some perforations remain dry for long periods, a patient with chronic perforation of the eardrum should be referred to an otolaryngologist for definitive repair to prevent cholesteatoma.

Otitis Externa

Otitis externa (swimmer's ear) is the most common cause of ear pain in teenagers. The cause is a combination of mechanical obstruction to drainage of bathing water from the external ear

canal and an infectious agent, almost always bacterial. Predisposing skin conditions include eczema, seborrheic dermatitis and psoriasis involving the ear canal. External otitis may occur secondary to drainage from the middle ear through an acute or chronic perforation of the eardrum. The bacterial causes are *Pseudomonas*, *Enterobacteriaceae* or *Proteus* species. Fungus infection is rare and when present, less acute.

Clinical Manifestations

Ear pain sets on over a few hours and is associated with tenderness that is readily elicited by graduated digital pressure on the tragus or by traction on the auricular appendage. In severe cases, the appendage may be red or edematous with cellulitis. Otoscopic examination reveals a canal narrowed or obstructed by swelling and possibly filled with purulent debris. Presence of a perforation of the eardrum may be deduced by history suggesting prior middle ear infection.

Management

Treatment consists of various topical combinations of acetic acid, usually 2% (e.g., VoSol otic solution). For effective access by the medication, the ear must be cleared of excessive debris. This may be done gently with an ear loop, though a gentle lavage is often the most acceptable method, assuming no eardrum perforation. This may be a more complicated problem if cerumen impaction is the main cause. In more severe cases various antibiotic solutions are effective, such as combined polymyxin B and neomycin (Polysporin Otic). When medication is denied access because of edema of the canal, a wick may be placed, typically a 1/8-inch wide, 1½-inch long section of umbilical tape soaked with the prescribed medication, inserted with bayonet forceps and followed with a cotton pledget at the external orifice. Colistin otic drops 3 mg/ml (Colymycin), while more expensive, is significantly more effective than more conservative preparations, as measured by the need for fewer follow-up visits and less required lavaging. Most cases are significantly improved within 2 days, the recommended follow-up interval in moderately severe disease. Any reaccumulation of cellular debris is lavaged out. The average course of topical treatment is 5 to 7 days in uncomplicated cases.

Topical glucocorticoid may be added to the foregoing, most appropriately in cases that complicate seborrhea, nummular

eczema or contact dermatitis. Hydrocortisone 1% may be prescribed in brand-name products such as VoSol HC, Cortisporin or Colymycin S otic drops. For dry processes, often pruritic and painless, the most appropriate vehicle may be a cream or even an ointment base. In cellulitis, a systemic antibiotic is included, usually ciprofloxacin or an antipseudomonas penicillin for a standard 10-day treatment. Recurrent otitis externa may be prevented by instillation of 2 drops of antiseptic alcohol solution or a preparation such as acetic acid 2% prior to swimming.

Malignant external otitis is an entity that evolves from persistent external otitis in a diabetic or immune-compromised individual. By definition it is complicated by osteomyelitis of the floor of the bony canal and/or mastoid and contiguous bones. Granulation tissue is usually visible in the canal at the site of the original bony involvement and a foul odor emanates from the discharge. Patients are admitted for otolaryngologic management and parenteral antibiotic therapy.

Bullous Myringitis

This is an unusual entity consisting of painful bleb formation on the external aspect of the eardrum associated with some colds, influenza and mycoplasma infections. The symptoms are difficult to distinguish from those of classic otitis media. Coryza may occur as with the common cold (or less so with influenza), followed in a few hours or days by earache. The eardrum appearance may be confused with that of otitis media. In the absence of true otitis media, the drum may be demonstrably mobile during the modified Valsalva maneuver or upon air insufflation into the external canal under a closed otoscope head. The condition is the result of the primary infection, rather than a complication. The patient should be treated empirically to cover mycoplasma with erythromycin, other macrolide antibiotic, or a tetracycline.

Non-otic Complaints of Ear Pain

Referred Pain

No hearing loss occurs, the Weber test does not lateralize, and the drum is mobile. Ear pain is often the presenting complaint of early viral pharyngitis, with eustachian tube referral to the ear. Dental problems, particularly upper molar disease, cause pain

that is referred to the ipsilateral ear. The offending tooth is tender to percussion by the end of a tongue blade. There may be vague ear pain associated with laryngeal or esophageal cancer. It is typically preauricular in location.

Temporomandibular Joint (TMJ) Syndrome

Pathogenesis. This is a common cause of ear pain, though it presents more frequently as facial pain or as straight forward jaw pain. It may be a precipitating cause of vascular headache (Chapter 3). In a busy practice, one or two patients require a series of visits for this complaint in a year's time. Three-fourths are in females between the ages of 25 and 40. Two ingredients are required for genesis of this syndrome: malocclusion and bruxism. Bruxism may occur in wakefulness or in sleep. It is generally a manifestation of emotional tension of which the patient may or may not be aware. A similar pain may arise less frequently due to chronic excessive tension of the muscles of mastication in the absence of malocclusion. In either syndrome, a palpable click in the TM joint suggests development of traumatic arthritic changes.

Examination of the ear is negative except for tenderness in the TM joint, which is palpable as the inferior rim of the bony canal at the external orifice. Prescribing nonsteroidal anti-inflammatory analgesics and addressing the fundamental causes is successful in 90% of cases. Patients should be referred to their dentists for evaluation and appropriate treatment of malocclusion. Relaxation training is helpful, as is cognitive therapy to teach the patient ways to avoid tension caused by non-constructive "self-talk" (Chapter 51).

Pain Caused by Inner Ear Problems

Inner ear problems can result in ear discomfort, but this is usually insignificant compared with the chief complaint, which relates to vertigo, tinnitus, and/or hearing loss, treated later in this chapter.

Otorrhea

The list of causes is chronic otitis media, the most common cause after cerumen; bloody discharge from foreign body; serous drainage from ruptured bullous myringitis; purulent discharge from external otitis; malodorous purulent discharge associated with cholesteatoma, and cerebrospinal fluid otorrhea associated

with basal skull fracture. The latter may be accompanied by the raccoon or Battle sign.

Hearing Loss

Hearing loss affects 5% to 7% of the total U.S. population; 13% to 23% of those between 65 and 74, and 48% of people over 84 years of age (7). Hearing loss may be subdivided into those of acute and chronic onset and further into conductive and sensorineural physiologic types. Sound intensity in decibels is measured exponentially, not linearly. Thus, doubling of decibel level is quadrupling of energy intensity.

Differentiating Conductive Versus Sensorineural Hearing Loss

Conductive hearing loss is due to impaired transmission of the sound along the external canal, across the ossicles and through the oval window. A sensorineural or perceptive loss is caused by an abnormality in the cochlea, the auditory nerve, the auditory projection, or auditory association areas. By history, the hearing loss is characterized especially by a deficit in discrimination; whereas a conductive hearing loss exhibits an increased threshold for perceived sound intensity (volume). At triage level they are usually differentiated by the tuning fork.

The Weber test is based on the phenomenon of "air conduction" of sound being better heard than bone conduction under normal conditions. In the Weber test, a tuning fork at 256 cps (or 512, if the room is quiet) is set into vibration and the stem held against the skull anywhere in the midline. A positive Weber test for conductive hearing loss is a demonstration that by bone conduction the patient hears the note better in the "bad" ear. A positive test for sensorineural hearing loss is the finding that the sound is heard better in the "good" ear. In case of hearing loss in both ears, the Weber test is invalid.

In the latter event the Rinne test applies. It is based on the same principle, but requires only one ear for testing and allows slightly weaker conclusions. The tuning fork is set in motion, and the patient allowed to hear the note through the external orifice. One way of performing the test is to allow the patient to listen to the subsiding sound with the prongs aligned with the canal at the orifice at a defined distance of 1 inch (2 1/2 cm) and instruct him/her to signal when it is no longer audible. At that point the

stem of the fork is placed on the ipsilateral mastoid bone, and the patient is asked whether the sound is again heard in the tested ear. If it is again heard, bone conduction is better than air conduction and the patient has a conductive hearing loss on the tested side. If the sound is not heard when the stem is placed against the mastoid, air conduction is better; i.e., normal physiology or ipsilateral sensorineural loss.

Problems Characterized by Conductive Hearing Loss

Middle ear disease diagnosis and treatment have been cited as always being characterized by a conductive hearing loss.

Obstruction of the External Canal. *Impacted cerumen* occurs to an extent that impedes visualization in about 10% of healthy young adults. In a primary care setting the cerumen may be delicately removed with a wire loop or cerumen spoon, generally best done when the wax is formed in a single or few fragments. More often, to avoid pain in the sensitive external canal, lavage is preferable, with a pressurized irrigation stream or a simple ear syringe. The tympanic membrane must be intact for safe lavaging.

The cerumen may need softening by pretreatment with H_2O_2 solution or triethanolamine polypeptide oleate (Cerumenex). Several drops are instilled and allowed to penetrate for 15 minutes before lavaging. With a cerumen syringe equipped with a shield to prevent spraying, the stream of water at skin temperature (to avoid precipitation of vertigo) is directed, sometimes firmly, in pulses along the superior wall, allowing the returning stream to carry out the cerumen into a kidney shaped basin. The maneuvers are continued until the return is clear. If unsuccessful, the physician may prescribe the drops for the patient to instill at home every 6 hours, each time washing out the canal after 30 minutes. The patient returns for repeat of the lavage in an outpatient setting the next day and sometimes, a third day as well. When the process has been traumatic, it is wise to treat the patient for a few days with topical solutions to protect against external otitis.

Hearing loss caused by *acute external otitis* occurs rarely when edema or exudate is sufficiently severe to occlude the canal. Management of external otitis is discussed later.

Otosclerosis (tympanosclerosis) is a cause of conductive hearing loss usually amenable to surgical correction. It is caused by abnormal new bone formation in the oval window and elsewhere in the labyrinthine capsule. It appears to be inherited as an incompletely

penetrant autosomal dominant trait and has a racial predilection for caucasians with histological prevalence in as many as 12% and symptoms in 0.2 % of the population. It is much less prevalent in Africans and nonexistent in Asians. Pregnancy causes acceleration of the process, and females with symptoms outnumber males approximately 2:1. Conductive hearing loss first occurs in young adulthood, reaching a significant degree in middle age. Eventually, labyrinthine capsular involvement leads to sensorineural loss as well. Diagnosis is suspected when a conductive hearing loss occurs in the face of normal otoscopic findings and absence of a history suggesting infectious middle ear disease. Surgical treatments can restore hearing to within 90% of the bone/air conduction gap.

Problems Characterized by Sensorineural Hearing Loss

This section deals with Ménière's syndrome, noise-induced hearing loss (acute and chronic), presbycusis, drug induced hearing impairment, hearing loss from viral infection, hearing loss associated with cerebellopontine tumors, and sudden unexplained hearing loss. It is impossible to discuss sensorineural hearing loss without considering problems associated with vertigo, discussed later in this chapter.

Presbycusis. This is by far the most common cause of hearing loss in the developed world and occurs with age in most people, males more severely than females. Measurable as early as the 20s and 30s, it becomes symptomatic in an increasing proportion of the population over 50 years. It usually involves the higher frequencies and early is associated with high-pitched tinnitus. Cross-cultural studies indicate that it is more often caused by noise exposure, albeit in people with inherently heightened sensitivity. Difficulty in discrimination is the most common subjective complaint. With a person who has this type of hearing loss speaking more slowly rather than louder is effective. Hearing aids, though more helpful in conductive hearing loss, are applicable in presbycusis as well, and newer technology has provided them in smaller and less obtrusive packaging.

Ménière's Disease (Labyrinthine Hydrops). This is a relatively common problem in primary care, not counting presbycusis, accounting for perhaps 10% of acquired chronic hearing loss. The syndrome of labyrinthine hydrops occurs in attacks resulting in hearing loss and vertigo of peripheral origin. The vertigo may be associated with nausea and vomiting. The attacks last from minutes

hours, but unsteadiness may persist for longer. The hearing loss, though abating with each attack, resolves incompletely, leaving always a residual and eventually significant deafness in the absence of successful preventive therapy. The residual perceptive hearing loss may involve only the lower frequencies of the conversation band. The attacks of dizziness are true vertigo (rotatory sensation) but do not require motion for precipitation. They may be quite violent and associated with nausea and vomiting. The severest phase lasts only a few hours and is worst in the earlier part of the course, diminishing as sensitivity of the inner ear decreases with the accumulative damage of repeated attacks. Attacks may be as frequent as weekly but are usually once or twice per year. Less severe variants exist, and some cases consist of bouts of tinnitus or temporary dampening of hearing without vertigo. Otolaryngologic consultation is warranted with the first attack.

Many cases can be managed reasonably well with diuretics and salt restriction, based on one of the theoretical causes: increased permeability of Reissner's membrane, resulting in sodium from the perilymph of the scala vestibuli entering the endolymph of the scala media, causing distention. This condition is called *labyrinthine hydrops*. A few patients may require surgery, which may vary from conservational to obliterative, depending on the extremity of the vertigo and the relevance of residual hearing preservation. Reversible aggravating causes of labyrinthine hydrops include hypothyroidism, uncontrolled diabetes and adjacent (middle ear) infection.

Acoustic Trauma and Noise-Induced Hearing Loss. Acute acoustic trauma occurs with sudden loud sound, such as explosions, or prolonged painfully loud noise (130 db or louder) such as a rock concert. A sufficiently powerful explosion may result in ruptured eardrum and mixed perceptive and conductive hearing loss. Typically the ears feel as if they were stuffed with cotton for 12 to 48 hours afterward, during which audiometry or tuning fork testing in the relevant frequencies would show a perceptive hearing loss. Repeated episodes result in permanent loss, as may a single loud noise, such as a rifle shot.

Chronic exposure to noise below the pain threshold is a more common cause of noise-induced hearing loss, as in factories, flight lines in aviation settings and outdoor equipment. The allowable limit established by the Occupational Safety and Health Administration (OSHA) for 8 hours of exposure per day is 90 db. If exposure exceeds 85 db regularly, the worker must be

monitored in a hearing conservation program. Among workers, hearing protection has become routine in noisy occupational environments. The hearing loss is perceptive in type, and the audiometric changes occur first at around 4000 cps. As the noise trauma accumulates, the decibel loss at 4000 deepens and adjacent frequencies become involved, producing a "V" in the standard audiogram.

Cerebellopontine Angle Tumors. Acoustic neurinomas make up 78% of cerebellopontine tumors. Incidence is 1/100,000; female:male ratio is 1.5:1. Ninety-five percent are unilateral (8). Fifty-one percent of cases present as hearing loss, and many have been misdiagnosed as otitis media, based on a perceived color change in the eardrum. The Weber test indicates a sensorineural hearing loss. Sixteen percent come to the doctor because of tinnitus without hearing loss, 9% because of subjective dizziness, unsteadiness, or vertigo. More advanced cases cause space-occupying symptoms such as trigeminal nerve dysfunction, visual complaints, or facial weakness. When bilateral (2% to 3%), they evoke the likelihood of von Recklinghausen's disease. Other tumors of the cerebellopontine angle are meningioma and cholesteatoma.

Diagnosis is made by high resolution CT or MRI scans after suspicion is heightened by onset of sensorineural hearing loss in conjunction with vertigo of the central type. Audiometric studies reveal such loss occurring first in the high frequencies and problems in discrimination. Treatment is neurosurgical and is more successful the earlier the neuroma is diagnosed.

Drug-Induced Sensorineural Hearing Loss. The drugs most well known for this problem are streptomycin, kanamycin, neomycin, and ethacrinic acid, for which reason they are seldom used clinically. The onset is often insidious and may be delayed. Tinnitus is the usual first symptom. Hearing loss is initially in the high frequencies and may go unnoticed unless tested for by audiometry. Decreased caloric response is usually found as well. The keys to prevention are knowledge of the drugs' side effects, using drug levels when appropriate, baseline audiograms, alertness to the first symptom of tinnitus and liberal use of follow-up audiograms.

Sudden Unexplained Hearing Loss. This is not a rare occurrence in primary care, and little progress has been made in its understanding over the past 20 years. In adults, it appears to occur most often in the middle years, in males more often than females. It probably

has more than one cause, and possibilities include thrombosis of the internal auditory artery, a single episode of Ménière's disease and subclinical mumps. It is an emergency, and although the majority of cases result in permanent, complete hearing loss in the involved ear, many patients can regain varying amounts of hearing within a few weeks of onset. Otolaryngologic sources state that treatment is most propitious if instituted within the first 48 hours. This consists of bed rest, heparin anticoagulation, intravenous histamine, and vasodilators such as nicotinic acid.

Other Causes of Sensorineural Deafness. Sensorineural hearing loss in infancy and childhood include congenital causes, such as asphyxia, erythroblastosis, and maternal rubella. Acquired problems include measles, mumps, pertussis, meningitis, influenza, labyrinthitis, and rarely inner ear extension of otitis media.

Hearing Aids and Cochlear Implants

Hearing aids are battery operated amplifiers that are placed in proximity to the ear, raising the intensity of sound by 70 db. The average level of conversation is 60 db. Models vary from small in size, nearly hidden within the external canal and more expensive, to readily apparent and less expensive. In general, conductive hearing loss is more amenable to hearing remediation, while sensorineural loss with its attendant discrimination problem is less so. Cochlear implants have been developed and apply to certain candidates who have suffered total hearing loss after having normal hearing and speech development.

Dizziness, Vertigo, and Inner Ear Problems not Involving Hearing

Dizziness is a name given by patients for a variety of symptoms. Besides vertigo, it may signify malaise, postural lightheadedness and other near syncopal episodes. The latter are discussed elsewhere.

Dizziness as Vertigo

True *vertigo* may be a spinning sensation, or less often a turning or rocking. It is caused by irritative phenomena involving the labyrinth or the central nervous system (8th cranial nerve, brainstem, cerebellum or temporal lobe).

Vertigo of peripheral origin by definition originates in the labyrinth. It tends to be precipitated by motion, exhibits *fatigabil-*

ity and a period of *latency*. Latency is defined as delay between the precipitating motion and the onset of vertigo and its sequelae, usually 3 to 20 seconds but possibly as long as 1 minute. Vertigo of peripheral origin is characterized by nystagmus that has both a slow and a fast or beating component, which points *away* from the effected side. Fatigability is the tendency to occur with less intensity and frequency with repeated bouts of motion.

Centrally caused nystagmus tends to be pendular, i.e., with a symmetrical motion that is fastest in the midpoint of the swing. Some vertigo of central origin may be motion related but does not exhibit latency nor fatigability. Central vertigo that is motion related may constitute another exception in that its nystagmus has both a fast and a slow component. When that occurs, the fast motion points *toward* the side of the lesion. Further, some peripherally caused vertigo may be spontaneous, i.e., not precipitated by motion, e.g., Ménière's.

Nystagmus of peripheral origin tends to subside when the gaze can be focused on a stationary point (as seasickness is often alleviated by gazing out at the horizon). Nystagmus of central origin will not subside upon gaze fixation.

Testing for Central Versus Peripheral Vertigo. The Hallpike maneuver consists of activating all three semicircular canals simultaneously by having the patient lie down and turn the head 90 degrees in one rapid motion, then observing the eyes as the patient gazes at a blank panel. If no nystagmus occurs by the end of 1 minute, the dizziness may not be true vertigo. If nystagmus appears with both slow and beating components after a latency period (usually of 3 to 20 seconds), the vertigo is of peripheral origin.

If there is immediate onset of nystagmus (and usually vertigo) the vertigo is of central origin. Other types of central syndromes may manifest vertigo and nystagmus before the test is run so that the test is not applicable. The Bárány test is a variation in which the head is dropped over the end of the table.

Causes of Vertigo of Peripheral Origin

These are diagnosed by the described tests, and they respond with symptomatic relief from drugs such as meclizine or diphenidol (Vontrol).

Vestibular Neuronitis. This has traditionally been called labyrinthitis, probably caused by a viral infection of the labyrinth. It is self-lim-

ited, causing vertigo without hearing loss, and is characterized by violent motion-induced vertigo lasting for a period of days to weeks.

Labyrinthitis. This taxonomic term is now reserved for conditions involving purulent or erosive processes, which are much less common than vestibular neuronitis (9).

Meniere's Disease. The pathophysiology and management have been discussed.

PHARYNGITIS

When defined as a symptom of pain, it ranks 4th and makes up 2.5% of complaints leading to office visits (1). Sixty-two to ninety percent of cases are caused by viruses, depending on the epidemiologic setting. Streptococcus accounts for 5% to 38% of cases of sore throat (10), depending on the time of year, the epidemiologic state of the community, and the conditions of crowding of the subpopulation in question.

Bacterial (Streptococcal) Pharyngitis

There are only a few etiologic causes of bacterial pharyngitis, and virtually just one. Diphtheria disappeared after the advent of vaccination in the 1940s; gonorrheal pharyngitis was seen commonly in the 1970s and remains in the differential diagnosis of sore throat; tularemia is a rare cause of exudative pharyngitis. Hemophilus influenza rarely causes epiglottitis in both children, in whom it may cause sudden laryngospasm, and in adults, wherein that complication is less likely.

The foregoing aside, virtually all cases of bacterial pharyngitis in the United States are caused by beta hemolytic streptococcus pyogenes. Though more than 90% to 95% of pharyngeal streptococcal disease is caused by Lancefield group A; groups C and G have been associated with exudative pharyngitis, as well. The latter may account for a portion of the 10% \pm false negative rate observed for the rapid strep tests based on Group A-specific antigen/antibody agglutination or enzyme immunosorbent assays.

Streptococcal Pharyngitis in Children. The main concern with this disease in children is the risk of poststreptococcal disease. Rheumatic fever incidence subsided from 250,000 cases in the 1950s to near extinction, only to rebound somewhat during the 1980s (11). Rheumatic fever is preventable if beta hemolytic

streptococcal disease is treated within 7 to 9 days of onset (12). The originally observed attack rate for untreated children was 0.3% (10).

Poststreptococcal glomerulonephritis is preceded by impetiginous skin infections at least as often as pharyngitis and has been reported after *S. pneumoniae* infection as well. Glomerulonephritis is apparently not preventable by antibiotic treatment of acute disease.

The pharynx is the normal habitat for beta hemolytic streptococcus. The recovery period of acute disease is said to be the most communicable time for passage from person to person, especially in crowded conditions such as military camps. The second most common mode of spread is through contaminated foods.

Physical Findings and Predictability of Streptococcal Pharyngitis. Tonsillar exudate, tender swollen anterior cervical lymph nodes, and history of fever are presumptive of strep pharyngitis in the presence of sore throat without cough or coryza. Other presumptive signs are palatal petechiae and exudate elsewhere in the pharynx. The probability of a positive throat culture in the presence of pharyngitis is 43% where strep disease is prevalent. It is reasonable to treat empirically with antibiotics, if the foregoing conditions obtain, particularly when community prevalence is high.

Differentiation from Viral Pharyngitis. Exudative pharyngitis occurs in viral diseases, but is usually differentiable by the lack of tenderness or palpability of cervical nodes and the presence of other findings associated with viral disease. The vast majority of viral exudative pharyngitis is caused by infectious mononucleosis, which presents often with severe sore throat and even difficulty in swallowing saliva. Generalized adenopathy often occurs, and cervical nodes, though impressive, are generally without tenderness. The rapid slide test for Epstein-Barr virus is negative until 5 to 7 days after the onset, so that empiric antibiotic treatment is justified in severely symptomatic cases. Cytomegalovirus infection causes an exudative pharyngitis indistinguishable from infectious mononucleosis, and is considered in the face of persistent seronegativity for mono. Ulcerative pharyngitis is caused by coxsackivirus A and by herpesviruses (13).

Diagnosis. Rapid screening tests based on immediate antigen detection exhibit an 80% to 87% sensitivity and 90% to 96% specificity (14, 15). Throat cultures, requiring 1 to 2 days of incuba-

tion, show a sensitivity of 90% to 95% and a specificity that approaches 100%, with the caveat that laboratory positive tests may be clinically falsely positive due to the carrier status in streptococcal disease.

Treatment. The pediatric literature of the last 15 years has stated that streptococcal pharyngitis is self-limited, running a 5- to 7-day course without treatment, and that antibiotics serve only to prevent rheumatic fever. However, the literature before the advent of antibiotics reported a mortality due to streptococcal disease ranging from 1% to 3% (15).

Penicillin remains the first-line drug and is best given as V potassium penicillin because of its absorbability regardless of dose relationship to meals. For adults, penicillin V potassium (Pen VK) is dosed as 250 mg 4 times per day for 10 days. For children, dosages are prorated to body weight. In 20% to 38% of patients treated, penicillin fails to eradicate the streptococcus (13).

Viral Pharyngitis

Most pharyngitis, and by far the most non-exudative pharyngitis, is caused by viruses. Cases are generally distinguished by their lack of physical findings, other symptoms of a non-purulent and non-focal nature, such as malaise, coryza, cough, occasional gastrointestinal symptoms and/or adenopathy without impressive tenderness. The viruses most commonly involved in non-exudative pharyngitis are rhino-, influenza and parainfluenza, respiratory syncytial, coxsacki- and cytomegaloviruses in children; and a longer list in adults, including Epstein-Barr, corona-, herpes, adeno- and myxoviruses. Most viral cases fall into the realm of the common cold, usually caused by the rhinovirus.

Allergic Pharyngitis

This is covered in greater detail in Chapter 35. Often the only symptom of allergic rhinitis and hay fever is the complaint of sore throat not unlike that of with the first 3 days of viral pharyngitis in a cold. It is diagnosed by the persistence of the sore throat with or without coryza that does not progress through the typical phases of the uncomplicated cold. There is usually circumstantial evidence of atopic allergy, such as asthma in the present or past, family history of atopic allergy or seasonality to the current symptoms. The diagnosis may be confirmed by the empiric response to

H₁-blocking antihistamines. Nasally inhaled glucocorticoids may help as well.

Atypical Complaints Relating to the Throat

On unusual occasions, a patient may complain of sore throat that is based on muscle tension and is a part of cervical and shoulder muscle spasm. It is identified by the physical finding of tenderness along the sternocleidomastoid muscle rather than in cervical nodes. Mumps presents as jaw pain that may briefly masquerade as adenopathy.

SINUSITIS

Table 1.4 shows the ages of anatomic pneumatization of the sinuses. The maxillary sinuses are pneumatized at birth to 6 months; the frontals at one year, visible at 3 to 9 years on radiography; the sphenoids sometime before adolescence; the ethmoids are developed at birth.

Table 1.4.
Development of the paranasal sinuses.

<i>Maxillary Sinus:</i>	Arises as a prolongation of the ethmoid infundibulum	at 12 weeks
	Pneumatizes	at birth
	Reaches stable size at	18 years old
<i>Frontal Sinus:</i>	Arises from the upper anterior area of the middle meatus	starts at late fetal life or even after birth
	Pneumatizes	after 1 year
	Full size	20 years old
<i>Sphenoid Sinus:</i>	Arises from the epithelial outgrowth of the upper posterior region of the nasal cavity in close relation with the sphenoid bone	starts at 3rd fetal month
	Pneumatizes	during childhood
	Full size	15 years old
<i>Ethmoid Sinus:</i>	Arises from the evagination of the nasal mucose into the lateral ethmoid mass	6th fetal month
	Pneumatization completed	7 years old
	Full size	12 years old

Reprinted with permission from Lee KJ, ed. Essential otolaryngology. 2nd ed. Garden City, NY: Appleton and Lange, 1977:206.

Sinusitis in Adults

Sinusitis usually follows or accompanies viral upper respiratory infections. Drainage from the sinus is compromised because of edema of the ostium. A self-limited sinusitis occurs in more than 85% of viral colds, involving the maxillary sinuses in 87%; the ethmoids in 65%; the sphenoids in 39%, and the frontals in 32%. Clinical, purulent sinusitis, however, occurs as a concomitant or in the aftermath of 0.5% to 5% of colds. Childhood infections are described below.

Symptoms include a sense of pressure and pain aggravated by shifts in head position, mental dullness, occasional facial or periorbital edema, and purulent nasal and postnasal drainage. Physical findings include tenderness over or failure to transilluminate the frontal or maxillary areas, and visible drainage from the superior meati in the cases of sphenoid and posterior ethmoid sinusitis, or from the middle meati for all others. Table 1.5 lists the pain localization and/or referral patterns of the various sinusitides (16). Sinus x-rays are helpful to elucidate recurrent and chronic symptoms.

The bacterial pathogens involved in sinusitis are the same as for acute otitis media, though their relative frequencies vary; *S. pneumoniae*, *H. influenza*, and less commonly chlamydia, *Staphylococcus aureus* and *Moraxella catarrhalis*. In chronic sinusitis, the flora includes anaerobes, mostly *Streptococci* and *Bacteroides*, in up to one-fourth of cases.

Complications of acute sinusitis include orbital osteomyelitis, extra-ocular muscle palsies, cholesteatoma, and orbital cellulitis. Antibiotic treatment choices are amoxicillin first, 250 mg three times a day to 500 mg four times a day x 10 day; amoxicillin with clavulanate, cefaclor, or ciprofloxin for recurrences or failures.

Table 1.5.
Referral patterns of the sinusitides.

Frontal	Pain and tenderness over the medial portion of the superior orbit
Maxillary	Pain and tenderness over the cheeks
Anterior	
Ethmoidal	Retro-orbital pain ± tenderness over the medial orbit
Posterior	
Ethmoidal	Center of the head or occiput
Sphenoidal	Center of the head, retro-orbital, frontal without local tenderness

Sinusitis in Children

Ethmoid sinusitis occurs after the age of 6 months and half of cases occur before the age of 5 years, presenting not uncommonly as orbital cellulitis, a serious complication that demands immediate treatment. Maxillary sinusitis is seen after the first year of life, while frontal sinusitis is not seen until preadolescence. The most common clinical presentations in children are purulent nasal or post-nasal discharge, or persistent cough, malodorous breath and intermittent periorbital swelling. These are often accompanied by fever.

Treatment is antibiotic therapy. In sporadic cases, 7 to 10 days of therapy suffices. In severe or recurrent cases, it should be carried out to 3 weeks. The first line choice is amoxicillin 40 mg/kg/day in three divided doses. If beta-lactamase-producing organisms are suspected, or if the patient is allergic to penicillin, the following choices are available: trimethoprim/sulfamethoxazole (e.g., Bactrin), 0.5 mL/kg twice per day; amoxicillin clavulanate 40 mg/kg/day (except in penicillin allergic patients); erythromycin plus sulfamethoxazole 10 mg/kg four times per day. If there is no response within 48 hours, central nervous complications should be ruled out. Then one should consider sinus aspiration for therapeutic and diagnostic purposes, or referral for that purpose to an otolaryngologist.

Orbital cellulitis may be associated with abscess, extra-ocular movement, proptosis, edema and visual disturbance. The severity has been staged, I through V, from inflammatory edema in the medial or lateral eyelid to cavernous sinus thrombophlebitis and proptosis with globe fixation, severe visual disturbance, prostration and meningismus (Table 1.6). Stage I can be managed in an outpatient setting by the same regimen as for acute sinusitis. Stage II should be managed in the hospital by intravenous antibiotics (17). Other complications of sinusitis in children are frontal osteitis (Potts puffy tumor), cavernous sinus thrombosis, subdural empyema, brain abscess, and osteomyelitis.

Recurrent sinusitis, like otitis media, is most often associated with atopic allergy (5). Other cases are caused by jumping feet first into water, mechanical problems, such as septal deviation, nasal malformation or foreign body. Patients who have allergic rhinitis may benefit from intranasal cromolyn or glucocorticoid. Vasoconstricting drops or sprays are all associated with rebound edema if used more than 5 to 7 days (5).

Table 1.6.
Clinical staging of orbital cellulitis.

Stage	Signs
I Inflammatory edema	Inflammatory edema in medial or lateral eyelid; usually nontender with minimal skin change; no induration, visual impairment or limitation of extra-ocular movement. Outpatient management acceptable.
II Orbital cellulitis	Edema of orbital contents with varying degrees of proptosis, chemosis, limitation of EOMs, and/or visual loss.
III Subperiosteal abscess	Proptosis down and out with abscess beneath the periostium of ethmoid, frontal or maxillary bones (in descending order of frequency).
IV Orbital abscess	Abscess within the fat or muscle cone in the posterior orbit. Severe chemosis and proptosis; complete ophthalmoplegia and moderate to severe visual loss.
Cavernous sinus thrombophlebitis	Proptosis with globe fixation, severe visual disturbance, prostration and meningismus, visual loss in contralateral eye.

Modified from Chandler JR, Langenbrunner DJ, Stevens EF. The pathogenesis of orbital complications in acute sinusitis. *Laryngoscope* 1970;80:1414–1428.

EPIGLOTTITIS

Hemophilus influenza is the cause of this painful sore throat leading to epiglottitis, with its attendant danger of laryngospasm. The classic findings are toxemia in the presence of drooling because of the inability to swallow saliva; inspiratory stridor; cherry red epiglottis, and the thumb sign on a plain lateral view of the laryngotracheal area of the neck. Immediate treatment may entail securing the airway by intubation. If that situation is avoidable, treatment includes humidified oxygen by mask; racemic epinephrine by inhalation; intravenous ampicillin, and a glucocorticoid such as dexamethasone or methylprednisolone in high initial dosages, followed by rapid tapering as the patient passes the respiratory crisis, usually within 48 to 72 hours. The patient must be hospitalized and observed by the surgeon, who would be available for emergency tracheostomy. The patient can be safely discharged early, after subsidence of the epiglottal edema, though the course of ampicillin or amoxicillin (or amoxicillin/clavulanate) would have to be completed for a net 10 days.

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Problems of the Oral Cavity

*Ames F. Tryon and
Charles F. Streckfus*

SCHEDULE OF NORMAL ERUPTION

With the exception of the first permanent molars, tooth eruption patterns follow a mesiodistal gradient in both the deciduous and permanent dentitions. The three stages of tooth formation and eruption include development of the crown of the tooth, eruption into the oral cavity and root completion. In the deciduous dentition, crowns are completely formed from 1.5 months of age until 11 months. In the permanent dentition, the crowns are completed between the sixth and 20th years. General eruption patterns for the deciduous dentition are listed:

Mandibular and maxillary central incisors (7.5 to 9.3 months); mandibular and maxillary lateral incisors (11 to 13.2 months); maxillary and mandibular cuspids (15.6 to 16 months); maxillary and mandibular first molars (19.5 to 19.6 months), and mandibular and maxillary second molars (26.5 to 28 months).

The permanent dentition commences with eruption of the first molars (6.0 to 6.3 years); the mandibular and maxillary central incisors (7.2 to 8.5 years); the mandibular and maxillary lateral incisors (7.2 to 8.5 years); the mandibular and maxillary cuspids (9.7 to 11.6 years); the first premolars (10 to 10.7 years); the first molars (6 to 7 years); the second premolars (10.7 to 11.5 years); the mandibular and maxillary second molars (11.7 to 12.7 years), and the third molars, or wisdom teeth, (20 to 20.5 years).

Tooth eruption in the deciduous dentition is sometimes accompanied by pain and an increase in salivary flow. Pain associated with eruption usually occurs between the sixth month and second year of life and is related to pressure being exerted by the erupting crown as it presses against the overlying dense fibrous tissue. During this period infants are likely to be irritable and restless, fail to feed or sleep properly. It is thought that the increased salivary flow or drooling is related to the inflammatory condition created by the emerging teeth.

THE STAGE OF DECIDUOUS DENTITION (BIRTH TO 6 YEARS)

Abnormalities in Teeth, Gingiva, and Mucosa

Gingival Cysts

A significant number of neonates have some type of gingival cyst. Approximately 58.2% have Epstein pearls, which are mid-palatal microkeratocysts. In addition, 22.6% of neonates have Bohn modules, which are seen on the alveolar ridges and appear white in color. Eruption cysts are also common and appear as bluish dome-shaped elevations that cover the crown of erupting teeth.

Hyperplastic Maxillary Labial Frenulum

This condition is marked by an oversized labial frenulum that is broadly attached to the upper lip and has a strong fibrous band that attaches to the incisive papilla. Children with this condition often have diastemas between their upper central incisors. Surgical correction in the maxillary arch is seldom necessary but is done in cases where orthodontic treatment fails to close the resultant diastema.

Short Mandibular Lingual Frenulum and Ankyloglossia

Ankyloglossia occurs in 1:3000 to 1:2000 children. Many cases of "tongue-tie" will resolve without treatment. Other cases could impair speech, mastication, and the occlusion. Surgical intervention is usually not indicated unless a serious functional impairment occurs. In the mandibular arch, frenotomy and frenectomy procedures are indicated where periodontal status is compromised. A simple frenotomy procedure can increase tongue mobility.

Abnormalities of Eruption

Approximately 1:3000 babies have natal teeth (present at birth) or neonatal teeth (erupt during the first few days or weeks of life). This condition is often associated with a congenital syndrome of some type. The majority of natal and neonatal teeth are part of the normal dentition.

Premature eruption is caused by an accelerated physiological process or pathological alveolar bone resorption. Delayed eruption is often associated with syndromes such as Down, congenital hypothyroidism or cleidocranial dysplasia. Local causes are also possible. Variations in the normal eruption are also related to syndromes and systemic diseases such as erythromelalgia and hypophosphatasia.

Abnormalities of Tooth Number, Form, and Size

Children may have fewer teeth than normal (oligodontia or hypodontia) or more (supernumerary or hyperdontia). Hypodontia is common in children with ectodermal dysplasia. Complete anodontia is extremely rare. Variations in tooth size and shape frequently occur in hypodontia and hyperdontia but may also occur in children with the normal number of teeth.

Abnormalities of Tooth Structure and Appearance

A significant number of children exhibit variations in enamel and dentin development and appearance. Deciduous tooth enamel provides a permanent record of fetal and neonatal insult, while permanent tooth enamel records events that occurred during infancy and early childhood. In addition, enamel formation and tooth formation are related to a variety of syndromes and conditions such as amelogenesis imperfecta. Dentine deficits are usually of genetic origin and include dentine dysplasia and dentinogenesis imperfecta. Other disturbances that should be noted in this category include severe attrition, extrinsic staining caused by chemical agents and intrinsic staining due to genetic factors, tetracycline therapy and various systemic conditions. Tetracycline therapy in pregnant women and children during the period of calcification of the deciduous or permanent dentitions can cause pigmentation of the clinical crowns of the teeth. The deposition of the drug results from its chelating properties

with the formation of a tetracycline-calcium orthophosphate complex. Tooth discoloration correlates with the stage of development of the tooth and the duration of drug administration as it relates to the period of calcification. The larger the dose relative to body weight the deeper the pigmentation.

Gingival Overgrowth Conditions

Fibromatosis and other gingival overgrowth occur in a small percentage of children. Gingival fibromatosis may be idiopathic, caused by an autosomal dominant trait or be related to a known syndrome. Drug-induced gingival overgrowth is usually caused by phenytoin, cyclosporin, nifedepine, or nitrendipine. Oral hygiene, removal of drugs, or surgical removal are options.

Salivary Gland Disorders

During the deciduous dentition period children can exhibit a variety of salivary gland problems including tumors as well as non-neoplastic conditions. Acute and chronic sialadenitis is not uncommon, and sialolithiasis is occasionally seen. Salivary gland agenesis is rare, and xerostomia and sialorrhea are sometimes observed in children undergoing chemotherapy or radiation and who have poor neuromuscular control. Cystic lesions such as mucocles and ranulae (salivary duct retention cysts) can also be observed.

Dental Caries

With the widespread use of fluorides and other preventive measures the prevalence of dental caries among children has been declining. In areas where water fluoridation is not present and among children whose diet is high in refined carbohydrates or those who do not seek preventive dental services, the caries rate can be much higher. When destructive caries are seen in young children, one suspects some form of "nursing caries." Sweetened pacifiers or comforters can cause a condition called "honey-dummy" caries usually involving numerous anterior and posterior teeth. Prolonged bottle nursing with cow's milk or other liquids with fermentable carbohydrates may lead to carious lesions. High-frequency "at will" breast feeding can also be a cause.

Traumatic Injuries

During the deciduous dentition stage, 80% of the traumatic injuries are caused by child maltreatment, followed by dog bites

and falls. In addition, a significant number of injuries to children are self-induced accidents involving chemical and electrical sources. In cases of suspected child abuse one looks for fractured jaws, temporomandibular joint injury, intraoral lacerations, lip injuries, and thermal or chemical burns.

THE STAGE OF YOUNG DENTITION (7 TO 21 YEARS)

Dental Caries

Today, when carious lesions are found in this age group, it is usually related to the absence of adequate levels of water fluorides during the tooth formation stage, inadequate preventive care, poor oral hygiene, diets high in refined carbohydrates, and/or systemic conditions that make the enamel susceptible to the development of lesions. Examples of the latter are xerostomia caused by drugs, radiation therapy, or other factors that affect salivary flow.

The options available for treating dental caries in the adult population are too numerous to list. Advances in restorative techniques and materials have reduced the need for the extensive removal of tooth structure during tooth preparation, and new materials such as composites and porcelain veneers enable dentists to create more economical, natural looking esthetic restorations.

Periodontal Diseases

Gingivitis and periodontitis are often found in this age group. Poor personal hygiene practices and a lack of preventive dental services account for most of the periodontal conditions among young adults. When oral hygiene and preventive practices are not the causal factors for inflammation and destructive periodontal conditions, one should suspect systemic factors. Leukemia and neutropenia are often accompanied by gingivitis and stomatitis. Anemia and sickle cell disease do not have the same impact as leukocytic disorders but should be considered when recommending any type of periodontal therapy. Finally, a small percentage of AIDS patients can experience severe gingival and periodontal changes.

Sexually Transmitted and Bloodborne Infections

Gonorrhea is often the cause of pharyngitis and gonococcal stomatitis. A wide variety of lesions are seen, including isolated

ulcers, gingivitis, and membranous gingivostomatitis. Primary syphilis is accompanied by chancres in various locations in the orofacial area. The oral lesions associated with secondary syphilis include mucous patches and split papules, while tertiary syphilis may cause gummatous destruction of the palatal bones. Manifestations of congenital syphilis include hypoplastic defects in the permanent dentition such as notched incisors and mulberry molars, when the occlusal surfaces of the crowns are deformed.

Herpes simplex virus types I and II and CMV are often implicated in herpes labialis and gingivostomatitis. Primary herpes simplex gingivostomatitis and pharyngitis are common in high school and college students. Human cytomegalovirus (CMV) infection is extremely widespread and can cause oral ulcers, gingivitis, and gingival hyperplasia.

HIV positive patients, especially those with AIDS, exhibit a broad array of oral lesions. Among those most commonly found are fungal infections such as oral candidiasis, oral hairy leukoplakia, gingivitis and periodontitis, salivary gland disease, recurrent aphthous ulcers, and Kaposi's sarcoma. Specific treatment regimens are described for all these conditions (Chapter 29).

Habit Patterns

Young patients often have habits that affect the orofacial area. Chronic thumb-sucking often produces anterior malocclusions, the upper anterior teeth deformed outward and the lower anterior depressed. Nail biting and chewing on foreign objects can cause abrasions and wear on the crowns of teeth. The use of smokeless tobacco such as snuff can often result in periodontal disease and white lesions (leukoplakia) in the mucobuccal fold area.

Developmental Problems and Malocclusions

A significant number of young people have malocclusions, and many are disfigured or have functional problems. Self-esteem can be affected by class II (overbite) as well as class III (lantern jaw) malocclusions, along with crowded and displaced teeth. In some cases, these malocclusions are associated with other problems affecting adenoids, the nasal passages, mastication, and proper breathing. Mouth breathers often have enlarged adenoids and high palatal vaults.

Referral to orthodontists for malocclusion may be determined by the appearance and functional and emotional status of the patient. In any event, referral is indicated when the malocclusion interferes significantly with mastication or breathing.

Impacted Teeth

Impacted third molars (wisdom teeth) can cause a series of problems for young people. Pain, when present, often radiates, involving more than one cranial nerve. Intraoral inflammation and infection can also be associated with impacted third molars, especially when food particles become trapped between the crowns of these teeth and the overlying tissue.

ORAL PROBLEMS OF ADULTS 12 TO 64 YEARS OF AGE

Emergency Dental Situations

Advanced Cellulitis, secondary to caries, is a clinical situation usually associated with severe pain in the orofacial region and accompanying cellulitis in the infected jaw. This can be life-threatening. When the cellulitis extends to the superior border of the eye or to the ramus of the mandible, the patient should be immediately referred to an emergency department with an "on-call" oral and maxillofacial surgeon. *Impacted or erupting third molars* appear as swellings in the posterior portions of the upper jaws. The third molar problems occur more frequently in the mandible than in the maxilla. An abscessed impacted third molar causes severe pain and sometimes a low-grade fever. Treatment is usually antibiotics (penicillin V or erythromycin; 250 to 500 mg orally, four times a day) and referral to an oral and maxillofacial surgeon. The pathogen is invariably Group A beta hemolytic streptococcus. *Avulsed teeth* are a common problem among adults, often resulting from athletic participation or spousal abuse. If the tooth is immediately replaced into the socket *without washing and with minimal handling*, it will probably be retained. If more than an hour elapses, or the tooth is handled excessively or washed, the prognosis for retention is poor. *Fractured teeth*, if minor (chipped), present no major problem, and the patient can be placed on analgesics and referred to a dentist at his/her convenience. If the dental pulp is exposed, however, the patient should be placed on antibiotics (penicillin V or erythromycin; 250 to 500 mg orally, four times a day) and analgesics and referred to a dentist for

immediate treatment. At that point the practitioner will perform a pulp procedure and/or replace lost tooth structure with a crown or composite restoration. *Fractured jaws* can result from accidents and intentional trauma. Maxillary or mandibular fractures present with pain (preauricular in a condylar fracture), swelling, tenderness to palpation, malocclusion, restricted opening, deviation on opening, diplopia, or discrepancy in the contours of the jaws and orbits. The physician can control hemorrhage and prevent airway obstruction by employing a Barton bandage (figure of 8 supporting the mandible below and in front). The patient should immediately be referred to an oral and maxillofacial surgeon or an emergency room. A *dislocated mandible* causes inability of the patient to fully close the mouth, with only the posterior (molar) teeth in contact. A midline deviation is indicative of a unilateral dislocation. Reduction can be achieved by injecting 1% lidocaine in the temporomandibular joint area and in the insertion area of the lateral pterygoid muscle. Manual reduction may be effected by placing the thumbs on the external oblique line of the mandible lateral to the third molars with the fingertips under the chin. The thumbs press inferiorly and anteriorly while the fingers press superiorly. The composite motion is rotary and continued until the mandible is relocated in its natural position. A Barton bandage can be used to immobilize the mandible.

Dental Caries

Dental caries can appear as black spots on intact enamel and cementum. They can also have a “carrot-like” appearance in advanced stages. Dental caries can be caused by dietary habits (high carbohydrate intake), patient neglect, or as manifestations of the treatment of systemic diseases (head and neck radiation therapy). Arrested caries can be asymptomatic, and referral to a dentist elective. Active carious lesions associated with pain and cellulitis, however, can be *life-threatening* (see Emergency Dental Situations).

Gingivitis

It generally appears as reddened, erythematous gingival tissues that may bleed spontaneously. The malady can be attributed to diet, neglect, or systemic disorders. This common disorder responds well to treatment and can usually be controlled by good oral hygiene practices and regular preventive dental care. Gingi-

al inflammation that *doesn't respond* to treatment, however, may indicate the early stages of more severe systemic disorders. Linear banding near the crest of the gingiva can be a sign of *HIV* infection. Additionally, gingival swelling that does not respond to treatment may be symptomatic of a *leukemic* disorder.

Periodontitis

Periodontitis is the advanced stage of gingivitis in which alveolar bone destruction occurs. This is apparent when root surfaces of the teeth become visible upon examination. In most cases, the disease is treatable; however, loss of alveolar bone supporting the dentition *is not* reversible. Periodontitis despite good hygiene practices and use of health care services may be caused by a more serious systemic disorder. *Acute necrotizing ulcerative gingivitis* (trench mouth) exhibits an unmistakable fetid odor and a fibrinous pseudomembrane upon the gingival crests. The patient should be placed on antibiotic therapy for (β -hemolytic streptococcus and referred to a dentist for treatment and oral hygiene counseling.

Oral Mucosal Lesions

The Lips

The most common lesion of the lips is generally the *mucocele* or *mucous retention cyst*. The lesion is benign and usually caused by trauma. The disposition is referral to an oral surgeon for excision. *Recurrent herpes labialis* (cold sores, fever blisters, herpes simplex type I) appears initially as small vesicles on the vermillion border of the lip. The vesicles usually rupture, forming a yellow, crusted lesion lasting 10 days or more. Topical antivirals such as acyclovir are the usual mode of treatment, though their effect on the course is minimal to modest. *The chancre of primary syphilis* is a sexually transmitted lesion of the lips. It is generally a painless single lesion with a raised border and reddish color. The cure is by treatment of the systemic disorder. *Cheilosis* is a fissuring and scaling of the tissues at the angles of the mouth and the vermillion surfaces of the lips. The lesion is characteristic in edentulous patients and in avitaminosis (B-2, riboflavin). If the lesion persists, it may be due to a mycotic infection, usually a strain of *Candida* (perleché). The lesion should be cultured and treated with antifungals.

The Palate

Torus palatinus or *palatal tori* are benign, bony exostoses on the palatal region of the oral cavity. They are more common in women and pose no major problem unless the patient requires full dentures. *Pleomorphic adenoma* is a common benign lesion of accessory salivary glands arising primarily in the posterior portion of the palate. The lesion is a dome-shaped, firm swelling with overlying normal mucosa. The patient should be referred to an oral surgeon for biopsy and removal. *Petechiae of the hard palate* are associated with β -hemolytic streptococcal pharyngitis and infectious mononucleosis.

The Tongue

Glossitis is generally defined as an inflammation of the tongue that may be a primary disease or symptom of a systemic disorder. The causes of glossitis include mechanical trauma, infectious agents, irritants (tobacco, spices), mouthwashes, and dental restorative materials. Additionally, glossitis may be secondary to systemic diseases such as anemia (pernicious and iron deficiency anemia), avitaminosis (B-2), primary herpes simplex, tuberculosis, streptococcal infections, or be associated with skin diseases, which include lichen planus, erythema multiforme, Behçet's syndrome, aphthous ulcer, syphilis, and pemphigus vulgaris. The tongue may exhibit a reddened tip and edges. This may indicate incipient pellagra, pernicious anemia, irritation from excessive smoking, or a tooth with a rough surface. In the later stages of systemic causes, the entire tongue may become fiery red. Whitish patches may be indicative of *Candida*. *Geographic tongue* (benign migratory glossitis) is of unknown origin and appears as denuded smooth patchy areas of the tongue demarcated by curvilinear white lines. These lesions are not painful and can be treated with topical corticosteroids. *Median rhomboid glossitis*, consisting of a rhomboid-shaped smooth, reddish nodular area of the dorsal midline of the posterior third of the tongue, is now thought to be the end result of a *Candida* infection. Median rhomboid glossitis is treated with an antimonilial agent. *Hairy tongue* is a profuse overelongation of the filiform papillae. The condition is asymptomatic and is often associated with antibiotic therapy, fever, oxygen-liberating mouthwashes, or a reduction in salivary flow. Treatment is tooth brushing and treating the underlying cause. *Glossodynia* and *glossopyrosis* (burning tongue) are

Common complaints usually associated with a local irritant, such as new prostheses. However, if the condition is progressive, underlying systemic disorders (pernicious anemia, amyloidosis, diabetes mellitus) may be present.

Floor of the Mouth

Ludwig's angina is the sublingual extension of cellulitis to the submandibular space. The infection can result from an abscessed molar, infected extraction site, or root canal therapy. Treatment is by incision and drainage accompanied with antibiotic therapy. *Epidermoid cyst* is a lesion in the floor of the mouth. The cyst is usually palpable in the midline of the floor of the mouth and the mucobuccal fold. Treatment of the cyst is excision. *Dermoid cyst* is doughy to the touch and is generally located in the midline of the floor of the mouth. Treatment for this lesion is excision by an oral surgeon.

Buccal Mucosa

Koplik's spots appear during the late prodromal and early eruptive stages of measles (rubeola). They appear as tiny, grayish-white macules with red margins. *Irritation fibroma*, not a true neoplasm, is located on the buccal mucosa near the occlusal aspects of the posterior teeth, associated with trauma (cheek biting). Treatment is changing the behavior or excision. *Lichen planus* in the oral cavity almost always involves the buccal mucosa and occurs as red cutaneous papules with erosive areas. The mucosal lesions are erythematous with lacy or netlike, white striae, (Wickham's striae), bullous or erosive. The erosive form is the potentially more serious and should always be biopsied. Lichen planus is treated with topical steroids. *Pemphigus vulgaris* is seen most often in Mediterranean and Middle Eastern individuals and may appear in the oral cavity as a bulla. It demonstrates Nikolsky's sign, readily collapsing and forming an aphthous-like ulcer. A biopsy is required in order to differentiate it from other vesiculobullous lesions. The disease may be controlled with immunosuppressive drugs. *Mucous membrane pemphigoid* manifests vesiculobullous lesions that can become red, eroded areas with a necrotic white slough. The lesion is more common in women than men, with the gingival tissues being the primary site. Treatment is palliative, using topical steroids; in severe cases, systemic corticosteroids are

used. *Herpangina*, the febrile disease in toddlers, is characterized by vesicles in the posterior part of the mouth and is caused by Coxsackie viruses.

Salivary Glands

Inflammatory Diseases of the Parotid Gland

The most common disorder associated with the parotid gland is “mumps,” an infection caused by a paramyxovirus. The disease lasts 1 to 2 weeks, and treatment is symptomatic. Bacterial infections (*Staphylococcus aureus*) of the parotid usually produce a swelling with a suppurative discharge from Stenson’s (parotid) duct. Management consists of appropriate antibiotic therapy. *Sialolithiasis* produces swelling of a salivary gland and milky discharge upon palpation of the affected glands. Treatment is surgical removal of the stone and antibiotic therapy when indicated. *Pleomorphic adenoma* is a benign tumor of the salivary glands. It can be found in both the major and minor salivary glands, but is most common in the parotid gland. Unilateral painless, swelling is present in the parotid and the lesion feels “rubbery” to the touch. Treatment is excision. *Xerostomia* can occur with head and neck radiation therapy, Sjögren’s syndrome, chemotherapy, and treatment with systemic medications (antihypertensives, antipsychotropics). Treatment is palliative (artificial salivas, salivary stimulants, anti-caries control), or in severe cases (head and neck radiation therapy), with a sialogogue such as pilocarpine. *Sjögren’s syndrome*, more common in women than men, produces enlargement of the parotid glands, xerostomia, angular cheilitis, and atrophy of the filiform and fungiform papilla.

Generalized Oral Disorders

Stomatitis is generally defined as an inflammation of the oral cavity. It can be caused by infection, irritants, trauma, and toxic agents, or secondary to more serious systemic conditions (autoimmune disorders, avitaminous). *Candidiasis* or “thrush” is characterized by curdy, slightly raised, white patches with erythematous borders. The predominant clinical feature is the ability to strip off the white area exposing a raw bleeding surface. Thrush is commonly found in head and neck radiation therapy, antineoplastic therapy, long-term antibiotic and corticosteroid therapies, the immunosuppressed (HIV), and in xerostomia. Treatment for candidiasis con-

ists of nystatin oral suspension 400,000 U or clotrimazole 10 mg lozenges for persistent infections. *Oral erythema multiforme* consists of painful hemorrhagic, diffuse lesions of the lips and buccal mucosa accompanied by a high fever. Its etiology is unknown. The skin lesions have the classic target or “bull’s-eye” appearance and can be found on the palms, extensor surfaces, and genitals.

Recurrent aphthous stomatitis (RAS) may be quite troublesome. RAS conditions can be grouped into three types, including the minor aphthous ulcer (Mi AU), Major aphthous ulcer (Mj AU), and the herpetiform ulcer (HU). Eighty percent of all RAS are of the Mi AU type. Mi AU are generally located in the buccal, labial and alveolar mucosa, the ventral surface of the tongue, the soft palate and the tonsillar pillars. In contrast, Mj AU are located throughout the mouth, including some of the more heavily keratinized areas. The etiology of RAS is poorly understood, but heredity, stress, and trauma are often implicated. Treatment for Mi AU or Mj AU includes stringent oral hygiene, covering agents such as choline salicylate, antiseptic mouthwashes, topical antibiotics (2% tetracycline), rest, and hydration.

Oral Neoplasms

Premalignant Lesions

Leukoplakia can occur anywhere on the oral tissues. It is characterized by a white patch of tissue that does not peel off. It can be associated with trauma, tobacco usage, avitaminosis, poor oral hygiene, and excessive alcohol use, including mouthwashes. Removal of the etiological agent is essential. If the condition persists, a biopsy is mandatory. *Erythroplakia* is a red lesion that can occur anywhere in the oral cavity and usually cannot be associated with any other condition. This lesion requires biopsy and has a greater malignant potential than leukoplakia.

Malignant Lesions

Basal cell carcinoma may occur on the lip as a shiny papule. The small lesion slowly enlarges displaying a pearly border with telangiectasia and a central ulcer that exhibits crusting and bleeding. Treatment of the lip lesion is biopsy and referral to an oral maxillofacial surgeon for removal. *Squamous cell carcinoma* may develop in normal tissue or in association with solar keratosis, leukoplakias, and erythroplakias. This particular lesion is more prevalent among

heavy tobacco and alcohol users. The posterior lateral border of the tongue and the lower lip are two common sites for the lesion, but it can occur anywhere in the oral cavity. It is particularly dangerous when located on the posterior third of the tongue. Squamous cell carcinoma usually appears as a red papule or plaque with a scaly, often crusted surface. The invasive lesion becomes ulcerative with typical indurated rolled edges. The prognosis is good if detected in the early stages. The treatment is similar to basal cell carcinoma. *Mucoepidermoid carcinoma* and *adenoid cystic carcinoma* are malignant neoplasms of the accessory salivary glands located on the palate. Initially, both lesions are similar in appearance to the pleomorphic adenoma. They are firm, dome-shaped lesions with normal overlying tissue. However, as the lesion progresses, it appears erythematous with multiple small telangiectatic vessels. Spontaneous ulceration of the lesion is not uncommon. The ulcerated surface of the mucoepidermoid carcinoma may also exhibit a mucous secretion. The prognosis is variable, depending on the degree of histological differentiation and the presence of metastasis. Patients should be referred to an oral and maxillofacial surgeon for treatment.

ORAL PROBLEMS OF THE ELDERLY (≥ 65 YEARS)

The oral disorders that were discussed in the previous section concerning young adults can also be found in the elderly populations. The following section concerning aged adults is dedicated to disorders that are common, but not exclusive, to the elderly.

Receding Gingiva or Gums

This is a condition caused by chronic periodontal disease, trauma (hard toothbrushes), or is iatrogenic by dentistry. It is characterized by root exposure due to the loss of alveolar bone and the associated gingival attachment apparatus. If associated with periodontal disease, bleeding and possibly suppurative discharge may be present. The patient should be referred to a dentist for treatment, as the condition places the patient at risk for other oral disorders.

Root Caries

Root caries are cemental lesions of the dentition that can be found on the exposed root surfaces. Root caries can appear as

small black dots or can involve the entire root surface of the tooth. Treatment should be rendered by a dentist electively.

Root Sensitivity

Root sensitivity is a common condition wherein the patient complains of pain in the dentition when consuming hot and cold foods and fluids or breathing cold air. The patient should be referred to a dentist for root desensitization restorative therapy.

Edentulism

Edentulism is common among the lower socioeconomic portions of society where economic access to care is prohibitive. The major medical sequela are nutritional. If the patient can not afford prostheses, he/she should be counseled regarding alternative nutritious soft food diets.

Oral Lesions

Denture sores are painful, traumatic, ulcerative lesions associated with either new or ill-fitting dentures. Treatment is the removal of the prostheses and topical oral analgesics (orabase with benzocaine). The lesions heal within 1 to 2 weeks. *Denture stomatitis* occurs among denture wearers, most commonly on the palate, and is caused by ill-fitting dentures. The lesion is painful, red, swollen, and can be either smooth or granular. *Candida albicans* is usually associated with denture stomatitis. Denture stomatitis may occasionally be an allergic response to the acrylic denture material. Treatment is removal of the dentures, antifungal therapy, new dentures or rebasing of the old prostheses. *Denture hyperplasia* (epulis fissuratum, redundant tissue, denture injury tumor) is hyperplastic or redundant tissue located in the maxillary buccal vestibule or the mandibular retromolar pad area. Whenever a denture-related lesion is found, the patient should be referred to a dentist for evaluation of the prosthesis. The lesion may be excised in order to allow proper fitting oral prostheses. Iatrogenic dry mouth is the most common form of salivary gland dysfunction in the elderly. More than 400 medications have potential xerostomic side effects. The condition is reversible, and patients should be given alternative medications whenever possible. Otherwise, the patient should be palliated using saliva substitutes, salivary stimulants, and anti-caries regimens.

In patients undergoing head and neck radiation therapy and cytotoxic therapy, salivary gland hypofunction can be severe, and marked weight loss can result. Treatment with pilocarpine may be used to improve salivary function in individuals undergoing these therapies.

Temporomandibular Joint (TMJ) Disorders

Arthritis can involve the TMJ. TMJ arthritis may be caused by trauma, infection, and by rheumatoid and osteoarthritis (Chapter 1). Traumatic arthritis may result from acts of violence, accidents, or hyperextension resulting from tooth extraction. Treatment is symptomatic, using analgesics, restricted jaw movements, soft diets, and heat applications. Infectious arthritis of the TMJ is characterized by inflammation and limited movement of the jaw. The treatment includes antibiotic therapy and TMJ exercises. Rheumatoid arthritis of the TMJ is seen as painful swelling of the joint, with limited opening of the jaw. Ankylosis of the TMJ follows in the majority of patients. Treatment includes jaw exercises and anti-inflammatory medications. Primary Degenerative Joint Disorder is common among people older than 50 years and can involve the TMJ as well as other joints. Patients will complain of mild pain, crepitation, and stiffness upon opening. Joint involvement is usually bilateral with the disorder treated symptomatically.

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Headaches

Kurt Kurowski

PERSPECTIVE

Headaches are among the most frequent reasons for a patient to consult his/her primary care physician. They were the 16th most common principal reason for an office visit in the United States, according to the National Ambulatory Medical Survey of 1985 (1).

About 17% of adult female and 5% of adult males experience one or more migraines in a year (2). Tension or muscle contraction headaches are the most prevalent (about 70% of headaches presenting to family practitioners), with all the variants of migraine headaches being the next most prevalent.

PATHOPHYSIOLOGY AND SETTINGS OF COMMON PRIMARY HEADACHES

Headaches can be caused by contraction, distention, spasm, displacement, or inflammation of any of the pain-sensitive structures of the head. These include scalp, arteries, musculature, portions of the dura, and some of the cranial nerves (V, VI, VII), as well as the cervical nerves.

Tension Headaches (Muscle Contraction Headaches)

The pathophysiology of tension headaches is not clearly known. The headaches are associated with the emotional tension of conflict or ambivalence, fatigue, or ordinary levels of daily tension in the presence of other factors that lower the threshold for the stress response. They usually are preceded by identifiable muscle spasm in the head and neck region. Tension headaches occur typically in the frontal region, the occipital, or both, or are occasionally

retro-orbital. Clinically, tension headaches appear to occur in response to preconsciously learned adaptations to stress. The muscle spasm response may respond to reconditioning through counseling or hypnosis. Conditions that frequently increase susceptibility include cervical ligament strain (whiplash), cervical radiculopathy, sinusitis, viremia, and chronic anemias. Electromyographic studies have inconsistently shown increased action potentials in the scalp and neck muscles of patients with tension headaches, and blinded examiners have found significantly increased pericranial tenderness in patients with chronic tension headache; thus, the term muscle contraction headache. Some believe the muscle spasm is just a secondary manifestation of the patients headache. Many investigators feel that tension headache may represent just another variation of migraines. Serotonin may play a role, as platelet serotonin and plasma serotonin levels have been shown to be low in patients with chronic tension headaches (3).

Migraine Headaches

The exact mechanism that produces migraine headaches is unknown. They have traditionally been attributed to cranial artery dilatation, and agents that can be shown to abort migraine attacks all have vasoconstrictive properties. Classically, the headache is hemi-cranial, preceded by a period of vasoconstriction, which causes a transient neurologic symptom, the aura. Though this theory is currently in doubt (4), auras do precede 15% of headaches and vary from homonymous scotomas in both visual fields, the most common, to virtually any neurologic symptom that can mimic a transient ischemic attack. The aura lasts nearly always less than an hour.

Many investigators currently believe serotonin receptors play a more significant role in the pathogenesis (5). Platelet levels of 5-hydroxy-tryptamine fall at the onset of migraine attacks. Sumatriptan, an agonist at some serotonin receptor subtypes, has been shown clinically to be effective in aborting migraines. Dihydroergotamine, which also is an agonist of certain serotonin receptor subtypes, has also been shown to be clinically effective. Migraine headaches are three to four times more common in women, most often in the second or third decades, are often worse peri-menstrually, or during the first trimester of pregnancy, and are often made worse (although sometimes made better) by oral contraceptive use. Estrogens modulate some of the serotonin and beta adrenergic receptors, and this may be the mechanism for these observed changes (6).

Cluster Headaches

The exact mechanism that produces cluster headaches is also unknown. They share many clinical similarities with migraines, such as unilateral distribution, and many investigators feel their mechanism may be the same or similar because of this. The clinical setting contrasts with migraine. Cluster headaches are more common in males in their fifth and sixth decades, occurring frequently for a number of days before remitting for weeks to months.

CLINICAL APPROACH TO HEADACHES

History

The clinician's first goal is to differentiate primary headaches (tension, migraine and their variants, including cluster headaches) from secondary headaches.

Although tension and migraine headaches are the most common headaches of childhood (7), patients with migraine and tension headaches usually first consult a physician during their adolescence or early adult years. The patient may come to the office or emergency room because she/he has never experienced a headache like this before, but on further questioning will have a history of similar headaches in the past, dating back to early adulthood or even childhood, with this headache being different only by being more intense. This is a typical pattern for primary headaches. Intensity itself cannot be the only guide to seriousness, as migraine attacks and cluster headaches can be worse than those associated with mass lesions, for example. However, their pattern is one of hours to days of headaches with pain-free intervals, whereas the patient with a mass lesion will complain of an insidious onset of headaches with slow progression, occasionally reaching the point where the pain keeps him/her from sleeping. The pain may vary slightly during the day and night, but no symptom-free intervals occur, and the patient may never have experienced headaches before this onset.

Tension headaches are usually located in the occipital and posterior cervical areas but may be in a hatband distribution around the head or more generalized. They are worse with stress and often increase by the end of a work day. Associated symptoms, besides those seen with stress and depression (anxiety, fatigue, sleep pattern disturbances), are unusual. The intensity of the headache is typically not severe, and the patient has usually

self-treated with over the counter analgesics successfully in the past. Though headaches may become chronic, occurring on an almost daily basis, the patient will have pain-free intervals.

Migraine attacks present as a unilateral (rarely bilateral), throbbing pain in the frontotemporal or parietal areas, or may be located behind the eye. The pain sometimes radiates into the occiput or neck. The typical attack lasts for hours, usually less than 24. However, on the rare occasions, when it lasts for days, it is called *status migranosus* (8). A minority of migraine sufferers have *classic* migraines, thus an associated aura (neurologic manifestations 1 to 2 hours before headache). Auras are usually visual, with flashing lights or lines or scotoma formation being common. Some patients experience hemimotor or hemisensory disturbances, dysphagia, or even auditory or olfactory hallucinations. The majority of migraine sufferers have common migraines without aura. Even common migraine sufferers may notice vague sensations of euphoria, fatigue, or irritability hours before the headache begins. The pain of a migraine, although usually moderate in intensity, can be severe. The frequency varies from a few per year to several every week. The pattern may change significantly so that an infrequent sufferer may begin experiencing daily, severe attacks. Aggravating factors such as oral contraceptive use must be considered when this pattern change is noted, and one must observe for clues to an organic cause. Associated symptoms of nausea, emesis, and photophobia are common, and the patient often prefers to stay in a darkened room. The patient may be hypersensitive to sound.

Cluster headaches occur in sprees wherein a patient may notice daily headaches, sometimes even starting at the same time each day, for a few weeks and then become symptom free. The headaches tend to last less than a few hours, but may last 1 or 2 days. They are unilateral and often located around the eye, and tend to be associated with tearing, rhinorrhea and/or facial flushing on the affected side. The pain is intense and often has a penetrating quality.

Subarachnoid hemorrhage produces a headache of sudden onset and intense severity, often described as "the worst headache I've ever had." They may be associated with nausea and emesis, and the patient will be lethargic if not comatose. He/She may complain of neck pain and stiffness.

Arteriovenous malformations do not produce a characteristic type of headache and can sometimes mimic migraines. They pre-

ent most commonly with hemorrhage, but sometimes with seizures, headaches, or focal neurologic deficits.

Strokes are most commonly ischemic in origin, in which case patients will experience little to no headache but will notice their neurologic deficits. Hemorrhagic strokes can precipitate a severe sudden headache and may be associated with significant cerebral edema, but their neurologic deficits still predominate over the clinical picture.

Hypertensive headaches occur but may not correlate with the degree of blood pressure elevation. The headache is usually bilateral and may be generalized. The patient sometimes describes the headache as a sense of increased cranial pressure or simply "fullness" and predicts that his/her blood pressure will be "up."

Intracranial mass lesions produce a deep, dull, headache that is initially mild and slowly increases in severity over a course of weeks to months, eventually keeping the patient up at night or being noted upon awakening and possibly followed by focal neurologic changes and/or seizures. Postural changes and other activities that increase intracranial pressure will increase the headache.

Temporal arteritis produces a headache of new onset of moderate severity in a middle-aged or older adult. It may last days or rarely weeks before the patient seeks medical attention. The pain is often located unilaterally or bilaterally in the temporal area but may be more generalized. The patient may have noted associated mild fever or weight loss and may have acute unilateral visual loss and pain with opening and closing of the jaw. Temporal arteritis is frequently associated with polymyalgia rheumatica, in which case the patient may also have been experiencing proximal thigh and shoulder girdle pains and weakness.

Meningitis can present with fever, stiff neck, and an occipital or more generalized headache in the older child or adult patient. The headache is moderate to severe and associated with nausea, vomiting, and photophobia. The patient will typically show altered mental status with lethargy, or irritability. Associated seizures are common.

Encephalitis can present with similar symptoms as meningitis but usually the symptoms are less severe and the fever not as high (i.e., $<102.0^{\circ}$). The mental status is not as much affected, and the patient may have continued to attend work or school despite symptoms. The sensorium will be affected, but in some cases the effect is minimal. Associated seizures are common here as well.

Posttraumatic headache can be seen along with other symptomatology such as lightheadedness, vertigo, and visual changes in patients who have recently suffered head trauma, particularly if a concussion occurred as post-concussion syndrome. The headaches are usually mild and generalized and may last for weeks to months after the injury; rarely they last beyond 6 months.

Headaches secondary to a medication side effect generally begin as generalized mild to moderate headaches after starting a new medication. Virtually every medication has been reported to produce headaches, but some, particularly vasodilators such as nitroglycerin, prazosin, and hydralazine, are much more prone to this, as are certain nonsteroidal anti-inflammatory agents such as indomethacin. Medications may also predispose a patient to, or precipitate other types of headache. Examples are oral contraceptives and worsening migraine symptoms, or anticoagulant predisposing a patient to subdural hematoma or hemorrhagic stroke.

While maxillary and frontal sinusitis cause localized pain and often tenderness in *sinusitis*, sphenoid and posterior ethmoid sinusitis may be said to cause a form of headache, located deep in the center of the head or suboccipitally. The patient complains of nasal and/or postnasal drip and often has symptoms upon arising. A history of sinus infections in the past is usually found.

Acute subdural hematoma can present with headache as its chief manifestation, can be seen at any age, and is associated with head trauma, often closed. Chronic subdural hematomas are more often seen in the elderly in whom a clear history of trauma is not always present. Alcoholics are more likely to suffer subdural hematomas, possibly as a result of head injury while intoxicated. They may or may not recall the event. Patients with coagulopathies or on anticoagulant or thrombolytic therapy are also predisposed. Besides the headache, the patient may demonstrate confusion and lethargy and may have focal neurologic deficits such as hemiparesis or aphasia. The headache and other symptoms most often follow the injury or are noted in the first 1 to 2 days after the injury. Symptoms, however, may take weeks or even months to develop in the chronic form.

Trigeminal neuralgia or tic douloureux can produce unilateral facial pains in middle-aged or elderly adults and is more common in females. The pain follows the distribution of the trigeminal nerve or its divisions and may be aggravated by touch to the area or chewing. A chronic course with exacerbations and remissions is common.

Herpes zoster can produce pain for days before the characteristic vesicles occur that follow a dermatomal distribution. On detailed questioning, however, the patient will localize the pain in the scalp or skin and be able to differentiate this from a true headache. The patient will also report that the area of the scalp where the pain is located is hypersensitive to touch. Patients with facial and head pain confined to a unilateral dermatome should be questioned regarding previous evidence of shingles in these areas, as patients may suffer from postherpetic neuralgia for months after resolution of the rash.

A headache in conjunction with fever, weight loss, arthralgias, solar sensitivity, erythematous rash, pleurisy, or pericarditis may represent a CNS manifestation of *systemic lupus erythematosus*. This is more likely in an adolescent or young adult female. An antinuclear antibody titer is part of the initial evaluation in such a case.

Family History

Sixty percent to eighty percent of migraine sufferers have a family history of migraines. Familial predisposition is difficult to assess in tension headaches because of their great prevalence. Patients with frequent, chronic tension headaches often have some symptoms of depression and anxiety, and the physician will often be able to elicit a family history of these disorders as well. The familial occurrence of cerebral aneurysms is rare, though the clinician should be more concerned about this possibility if more than one family member has been affected (9). Only a few reports have been made of familial occurrence of arteriovenous malformations (9).

Physical Examination

Documentation of any temperature elevation is critical, as it rules out primary headache etiologies unless the fever is caused by a concomitant illness. While the need to check the blood pressure is obvious, most patients with elevated readings are asymptomatic, and the presence of an elevated blood pressure (BP) does not identify it as the cause of the headache. More marked elevations ($>160/95$) increase the likelihood that hypertension is the cause. In conditions of increased intracranial pressure, such as severe hemorrhagic stroke and acute subdural hematomas, the pulse becomes rapid and irregular, respirations become irregular, and blood pressure rises.

Mental status is usually affected in cases of subarachnoid hemorrhage as well as in meningitis and encephalitis. Patients usually show mental slowness and a dulled perception of the environment; they may be irritable.

Head and Face

The patient is examined for swelling or ecchymoses to indicate trauma. Face and scalp need to be examined for vesicles if zoster is a consideration. Tenderness may be present and even a mild nodularity to the temporal arteries in cases of temporal arteritis, but this sign needs to be interpreted with caution, as many patients with primary headaches will have some vague temporal area or even arterial tenderness. A flushed face with unilateral lacrimation and rhinorrhea is characteristic of a cluster headache. One should auscultate for cranial bruits to search for arteriovenous malformations. The best place to listen for them is around the orbit and over the mastoids. The absence of a cranial bruit does not rule out an A-V malformation.

Percussion of frontal and maxillary sinus areas may reveal tenderness in patients with sinusitis. Involved sinus cavities will not fully transilluminate.

Eyes

A transient Horner's syndrome can be observed rarely during a cluster headache and still more rarely in migraine. Papilledema can sometimes be seen when intracranial pressure has been significantly increased, especially in subdural hematomas if acute, and in severe hemorrhagic strokes. Since increased intracranial pressure is not an initial manifestation in subarachnoid hemorrhage, papilledema would not be expected. Hypertensive headaches are more likely in patients with malignant hypertension. Thus are seen flame hemorrhages, hard exudates, arteriovenous nicking, and, in severe cases, papilledema.

Neck

Evidence of meningeal irritation such as stiff neck, positive Kernings and/or Brudzinskis signs may be elicited in cases of meningitis and subarachnoid hemorrhage. Carotid artery bruits may indicate carotid artery occlusive disease and a predisposition to stroke.

Neurologic

Patients with intracranial mass lesions will show progressive focal neurologic changes as the mass enlarges. The specific signs demonstrated will, of course, depend on the tumor site. Focal neurologic deficits will be the primary manifestation of strokes, whether they are ischemic or hemorrhagic. Patients with classic migraine will sometimes experience visual prodromes with field defects or distortions and/or hemisensory or hemimotor symptoms or even dysphagia. The headache tends to begin as these prodromal symptoms fade (often over about 30 minutes), and usually by the time the patient seeks medical attention, the clinician will not be able to appreciate any deficits. Most cases of subarachnoid hemorrhage result from rupture of an aneurysm or bleeding from an arteriovenous malformation, although sometimes no cause can be found. The underlying aneurysm or A-V malformation may produce a focal neurologic deficit or seizures, but they usually first present with hemorrhage. Even with subarachnoid hemorrhage, the focal neurologic changes may be minimal and relate to the neuronal compression from the hematoma and/or secondary ischemia from vasospasm after the hemorrhage. In ophthalmoplegic migraine, oculomotor palsies may persist even after the headache. However, the clinician must first consider an aneurysm near the sympathetic plexus around the carotid artery, common locations for aneurysms, which may present with pain around the eye, and a third cranial nerve palsy.

Diagnostic Testing

The vast majority of the patients seen by the primary care physician will not require any laboratory testing or imaging studies to arrive at a diagnosis and to institute treatment.

A new onset of headaches in a patient over 50 years of age warrants a sedimentation rate (ESR). It is a nonspecific test and must be corrected for age and sex as follows:

$$\text{Men: ESR} = \frac{\text{age (years)}}{2} \qquad \text{Women: ESR} = \frac{\text{age (years)} + 10}{2}$$

Despite nonspecificity, marked elevations in the ESR (>90) are usually only seen in temporal arteritis, polymyalgia rheumatica, or tuberculosis. Patients suspected of having temporal arteritis on clinical grounds and with significantly elevated sedimentation

rates should be placed on high-dose prednisone therapy pending temporal artery biopsy, which will show destruction of the lamina elastica and the presence of giant cells in patients with the disorder (see management to follow).

A computed tomography (CT) scan of the head is useful if stroke is suspected, whether hemorrhagic or ischemic. A CT scan usually shows no abnormality in the first 3 days after an ischemic stroke but is useful to rule out hemorrhage, which shows abnormalities immediately. A CT scan is also indicated if subdural hematoma is suspected and in suspected subarachnoid hemorrhage, which would show blood in the intraventricular spaces in 80% to 90% of cases. If subarachnoid hemorrhage is suspected on clinical grounds, despite a normal CT scan, an atraumatic cerebrospinal fluid examination will show large numbers of red blood cells. A CT scan or MRI study of the brain is the diagnostic study of choice if an intracranial mass lesion or an arteriovenous malformation is suspected. CT scan or MRI of the head may show an aneurysm if it is greater than 1 cm in size, but cerebral angiography would be necessary to appropriately define an aneurysm before any surgical intervention.

Patient Management

Tension Headaches

The patient with tension headaches has usually self-treated similar headaches in the past with over-the-counter aspirin, acetaminophen, or ibuprofen with variable success. If these are effective and if the patient has no contraindication to their use, they should continue to be used.

For more severe episodes, a prescription for Fiorinal (50 mg butalbital, 325 mg aspirin, and 40 mg caffeine) may be useful. Especially with more severe and more chronic cases, situational stresses or elements of anxiety or depression are often present. Scheduled visits to discuss these issues in detail and their relation to the patient's headache may be useful. Some patients' tension headaches are best helped by small daily doses of antidepressants. Although expensive, biofeedback has also been shown to be effective. Virtually no tension headache is so severe as to require narcotic analgesics, and headache of such severity should alert the clinician as to the need to consider other etiologies. The chronic nature of these headaches also increases the risk of narcotic tolerance and abuse.

Migraine Headaches

Whether classic or common, the degree of severity can vary from mild to so severe that parenteral narcotic analgesics are necessary. If over-the-counter analgesics are ineffective or contraindicated, a vasoconstrictor such as sublingual ergotamine may be effective, taken as soon as possible in the headache course. Since this is not an analgesic, only migraine sufferers should respond to it, thereby confirming the diagnosis. It is contraindicated in peripheral artery disease, uncontrolled hypertension, ischemic heart disease, and pregnancy. It may produce nausea, vomiting, numbness, and paresthesia of the extremities. Some patients find the taste of the sublingual ergotamine unpleasant and prefer to take an oral vasoconstrictor such as Cafergot (ergotamine tartrate and caffeine) or Midrin (isometheptene mucate, a sympathomimetic amine vasoconstrictor with dichloralphenazone, a mild sedative, and acetaminophen). Because Midrin contains a sympathomimetic amine, it is contraindicated if the patient is also on a monoamine oxidase inhibitor. A Cafergot suppository is available to those who cannot tolerate formulations due to emesis and nausea with the migraine attack. Dihydroergotamine mesylate (DHE 45) is an alpha blocking agent with some vasoconstrictive properties and serotonin antagonism. Like other ergot alkaloids, it is contraindicated if the patient has known peripheral artery disease, ischemic heart disease, uncontrolled hypertension, or is pregnant. It is given by intramuscular injection and should not be combined with other vasoconstrictors. Sumatriptan (Imitrex) is a selective serotonin receptor subtype agonist. It is highly effective initially against migraine headaches, with about 80% of patients obtaining relief within 2 hours of a single subcutaneous dose (10). However, many patients notice that their headaches recur within the next 24 to 48 hours. Sumatriptan is contraindicated in patients with basilar or hemiplegic migraine. As a vasoconstrictor, it carries the same contraindications as sympathomimetic drugs and ergot alkaloids. Sumatriptan is contraindicated in patients with known or suspected atherosclerotic coronary or peripheral artery disease, in Prinzmetal's angina, or in those felt to be at high risk for these conditions. It is also contraindicated if the patient has received some ergot preparation (ergotamine, DHE metylsergide) within the last 24 hours. Oral Sumatriptan is now available and is expected to largely supplant subcutaneous delivery. A 25 mg tablet is given at

the onset or during the migraine, and this is taken again 2 hours later if significant headache relief has not occurred, up to a total dosage of 300 mg/day. It carries the same contraindications as SC Sumatriptan and other vasoconstrictors. The most common side effects are chest pain or paresthesias in an extremity. Patients with status migranosus may benefit from parenteral or oral cortisone in addition to one of the above agents and/or a parenteral narcotic. Patients on oral contraceptives may develop, or may have previously experienced migraine headaches exacerbated by this medication and may need to go to an alternative contraceptive method.

Prophylactic Therapy for Migraine Headache

A few patients suffer from very frequent, even weekly attacks and may benefit from prophylactic therapy to decrease the frequency and severity of future attacks. Beta blockers, such as propranolol, and tricyclic antidepressants, such as amitriptyline, taken daily, have all been shown to be useful for this purpose. Calcium channel blockers have also been used but are probably less effective. Methysergide is also effective as prophylaxis. However, this drug is decreasing in use because of the rare potential to produce retroperitoneal, pleural, or endocardial fibrosis. Because of this, drug-free one-month intervals are recommended after every 6 months of treatment. Specific prophylactic agent selection should be based on the patient's concomitant illnesses and side effect profiles. Biofeedback can be useful in situations in which medication needs to be avoided as much as possible, such as during pregnancy.

Cluster Headaches

These can be difficult to manage. Verapamil 120 mg 3 or 4 times daily has been successful during cluster episodes. Sometimes patients respond to sublingual ergotamine. Oxygen inhalation 8 liters/minute for about 15 minutes has also been shown to be effective. This should be avoided in patients with chronic obstructive lung disease, as it may lead to carbon dioxide retention/hypoventilation. Subcutaneous injection of Sumatriptan has been shown to decrease cluster headache in about 70% of those who received it (11). Some have concerns about giving SC or oral Sumatriptan to the typical middle-aged male patients who are afflicted, as many of the patients could have occult coronary artery disease.

Primary Headache Treatment Issues in Children

With children even more than with adults, narcotics are to be avoided in tension headaches. Sublingual and oral forms of ergo-amine with caffeine have been used with success against migraine headaches in children, but are more commonly used in adolescents. For chronic recurrent headaches, prophylactic agents such as propranolol, calcium channel blockers, and amitriptyline have been used in children and adolescents, checking side effect profiles to avoid any contraindications. For many children prophylaxis may be discontinued on trial after about 6 months.

Hypertensive Headache

The patient should be started on the appropriate anti-hypertensive medication, with headache resolution anticipated as the patient becomes normotensive. Outpatients should return in 1 to 2 days for follow-up, and patients with severe BP elevations or optic disc swelling should be hospitalized. Please refer to Chapter 7 for a discussion of the management of cerebrovascular disease.

Temporal Arteritis

Patients with suspected temporal arteritis who have a marked elevation of their sedimentation rate should be placed on high-dosage prednisone (60 to 80 mg/day) pending temporal artery biopsy, as these patients are at risk for progressive ophthalmic artery involvement and irreversible vision loss. Patients with temporal arteritis will experience rapid relief of headaches and polymyalgia rheumatica symptoms within 24 to 48 hours on this regimen. If biopsy confirms the diagnosis, the dosage is maintained for 1 to 2 months and then tapered as long as they are asymptomatic and their sedimentation rates remain normal. They usually remain on daily (not alternate day) doses of 2.5 to 15 mg for 1 to 2 years and sometimes longer.

The medical and surgical treatment of stroke, subarachnoid hemorrhage, AV malformations, aneurysms, and subdural hematomas are beyond the scope of this chapter.

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Problems of the Eye

*Linda Miller Savory, Michael A.
Krasnow, and Jack E. Terry*

THE OCULAR EXAMINATION

Visual Acuity

The Snellen visual acuity is determined with the patient wearing any corrective lenses and before physical inspection or instillation of ophthalmic medications or stains. In the event of unavailability of patient's lenses, having the patient peer through a pinhole occluder acts to correct for a refractive error in most circumstances. One should test each eye separately using an eye cover or the patient's own hand. If the eye is painful, a drop of topical anesthetic initially may need to be instilled.

The time-honored definition of Snellen visual acuity is that the number on top represents the distance at which the patient is able to identify the smallest letter(s) of a designated line while the number under the slash represents the distance at which the normal eye would be able to see the same line. Thus, 20/40 means that the smallest line that the patient is able to identify at 20 ft is identifiable by the normal eye at 40 ft.

External Examination

As the examiner approaches the patient, he/she should observe for any dermatologic conditions such as herpes zoster, rosacea, or contact dermatitis. The lids and palpebral conjunctive are inspected, observing for ptosis (drooping eyelid), ectropion (lid

turned out) or entropion (lid and lashes turned in), and proptosis (protruding eye). A reddened palpebral conjunctiva generally indicates an infection (e.g., bacterial, viral, or chlamydial) or an allergy. Deeper purple injection around the cornea is termed ciliary injection.

The periorbital areas are examined for preauricular lymphadenopathy, preseptal cellulitis, or an orbital cellulitis. Carefully palpate the orbital rims for step-off fractures.

An abnormal head tilt or turn should be noted, and the extraocular muscle motility in all eight cardinal positions of gaze should be assessed for paretic muscles. The Hirshberg reflex is an easy method to appreciate a strabismus. The normal reflection of light is located 0.5 mm nasal to the visual axis in *both* eyes. If the reflection in one eye is found to be located temporally 1.0 mm, then the patient is approximately 33 (1.5 mm X 22/mm) prism-diopters *esotropic*. Assess the pupillary responses for an equal reaction to direct and indirect light, carefully noting any anisocoria (difference in pupil diameter) or afferent pupillary defect.

The cornea should be carefully inspected for abrasions, haziness, ulcerations, or dendrites after instilling fluorescein stain, if indicated by a complaint of irritability, spasm or photophobia.

Internal Examination

An absent red fundus "reflex" may suggest a miotic pupil, severe cataract, corneal or vitreous opacity, or retinal tumor or detachment. The patient's pupils should be dilated with 2.5% phenylephrine or 1% tropicamide (Mydracyl) unless the anterior chambers are significantly shallow and the fundus and optic disc viewed in their entirety.

Confrontational Visual Field Examination

An effective procedure to test field loss is to sit immediately in front of and facing the patient. Then, while the patient is looking at your eye and you are observing his eye (the other eye is covered), ask the patient to correctly identify how many fingers you are holding up in different fields of gaze, held approximately 18 inches from the eye in the cardinal positions, 45° from the central visual axis. To test for peripheral field limits the examiner creates finger movements at the peripheral limits of vision, normally limited only by the patient's nose, brow, cheek and lateral orbit confines.

EYE EXAMINATION BY SPECIFIC EYE COMPLAINT

The Red Eye

Conjunctivitis

Viral Conjunctivitis. A viral conjunctivitis may be temporally associated with a recent upper respiratory infection or infection of siblings or coworkers. The patient complains of burning, tearing, redness, and a serous-type discharge. The agent is often an adenovirus as in epidemic keratoconjunctivitis (pink eye) or pharyngoconjunctival fever. The conjunctiva is usually significantly red and swollen with associated follicles or papillae. Vision is generally not affected, nor is there pain or pupillary involvement. An adenoviral conjunctivitis resolves spontaneously. The patient should be instructed to wash his hands frequently with soap and water and not to share towels.

Allergic Conjunctivitis. The red eye may be described by the patient predominantly as pruritic with a thick and ropy white discharge. These findings may occur primarily during the spring and fall pollen seasons. Nasal and sinus congestion, postnasal drip, headache and hoarse voice also may be present. A topical antiallergic agent such as levocabastine (Livostin), lodoxamide (Alomide), ketoraloc (Acular), or an ophthalmic decongestant-antihistamine combination (e.g., Vasocon-A Solution, Naphcon-A Solution) may be prescribed. Lodoxamide is a mast-cell stabilizer that requires more prolonged use for relief, but the other agents provide more immediate symptomatic relief.

Bacterial Conjunctivitis. This is caused most commonly by *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, or *Moraxella catarrhalis*. Gram-negative organisms are more commonly found in immunosuppressed patients admitted to the hospital. The patient will complain of a foreign body sensation, burning, and matting of the eyelids upon awakening. Vision is normal unless rendered cloudy by a thick mucous discharge. Antibiotics of choice include ciprofloxacin, polysporin/trimethoprim, sulfacetamide, tobramycin, or erythromycin or bacitracin ointments. Neomycin ophthalmic drops are not recommended for adults since at least 15% of patients using Neosporin will develop a Type IV hypersensitivity to the drops and thus perpetuate further redness and unnecessary therapy.

This must be differentiated from a spontaneous *subconjunctival hemorrhage*, a redness of the conjunctiva after a small blood

vessel has broken. A subconjunctival hemorrhage is caused by capillary shearing caused by a rapid motion of the head, as may be caused by a sudden sneeze or rubbing of the eye. Subconjunctival hemorrhage develops over minutes and resolves over a week or so. While the patient is upright, the erythrocytes tend to settle downward as the blood dissects through the tissue. As the pigment oxidizes it will turn yellow, green, and then brown. Subconjunctival hemorrhages, since they spare the cornea or anterior chamber, do not cause visual loss.

Keratoconjunctivitis Sicca or "Dry Eye." This is a common source of conjunctivitis. To assist in the diagnosis, it may be useful to perform the Schirmer's test by placing a paper strip inside the lower lid for 5 minutes. The test is abnormal if less than 5 mm of wetness appears on the wick. This condition is treated with artificial tears in the daytime and methylcellulose ointment overnight. It is most commonly associated with collagen vascular diseases (Chapter 27).

Iritis

The hallmark of *iritis*, *iridocyclitis*, or *anterior uveitis* is a red, painful eye with a limbal flush (circumlimbal injection) and photophobia. This flush is caused by dilation of the deeper and larger episcleral vessels near the edge of the cornea. The pupil is smaller (miotic) in the affected eye. The etiology may be infectious, autoimmune, or idiosyncratic. The patient should be questioned about fever, rash, weight loss, cough, joint or back pain, and oral or genital sores. Diseases associated with iritis include rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematosus, Crohn's or Reiter's diseases, ulcerative colitis, sarcoidosis, syphilis, tuberculosis, and Behçet's syndrome. The patient should be referred to an ophthalmic practitioner the same day.

Glaucoma

This term applies to increased intraocular pressure, which causes loss of vision. Generally, it occurs in acute or chronic forms. The former has a greater incidence in many Asian groups and in Alaskan Inuits, while the latter is the predominant form of glaucoma in European and African-Americans.

Angle-Closure Glaucoma. Patients with angle-closure glaucoma present with circumlimbal ciliary injection and a painful eye with a steamy or hazy cornea, a mid-dilated pupil and severely decreased

visual acuity. Patients prone to angle-closure glaucoma can be identified by a shallow anterior chamber. The examiner can determine this by shining a penlight from the temporal side to see if light traverses through the anterior chamber to illuminate the nasal aspect of the iris. If only the most temporal aspect of the iris is illuminated, this indicates a shallow chamber and likely a closed angle. Do not administer mydriatics to these patients. The patient should be referred to an ophthalmologist immediately.

Acute-angle closure is relieved by laser or surgical iridotomy. Other causes of angle closure include a mature cataractous lens, neovascular glaucoma, and ocular tumors, which block the trabecular meshwork. Acute-angle closure can be confused by the patient with sinus headache or abdominal distention.

Primary Open-Angle Glaucoma. This disorder, corresponding to the older term, chronic simple glaucoma, afflicts 2% of the U.S. population over age 40, with the prevalence rising throughout the decades of life. Primary open-angle glaucoma (POAG) is a chronic, asymptomatic, and potentially blinding disease. It is characterized by elevated intraocular pressure, peripheral visual field defects, and large optic nerve cup to disc ratios. The cup to disc (c/d) ratio refers to the ratio of the excavated area of the cup compared with the entire disc diameter. Some of the risk factors associated with primary open-angle glaucoma are age greater than 50 years, African-American race, and family history of glaucoma. The prevalence of POAG is 1.3% of whites and 4.7% of African-Americans.

Primary open-angle glaucoma can be screened by measuring the intraocular pressure (IOP) with a Perkins' hand-held or Schiottz tonometer on those patients older than 40 or at age 20 in African-Americans. IOP alone, however, may under-detect a great percentage of cases. Sensitivity is increased by combining IOP screening with assessment of the optic nerve head. Direct ophthalmoscopy should be performed to evaluate the optic nerve for any large c/d ratios (especially if vertically elongated, e.g., 0.6 horizontal and 0.8 vertical), which could indicate glaucomatous damage. A prompt referral and diagnosis of primary open-angle glaucoma can be beneficial in preventing further optic nerve damage and further vision loss.

Crusting Eyes

Blepharitis, or chronic inflammation of the lid margins, causes the eyelashes to adhere together. Warm compresses will allow the

lid to separate. Vision is not impaired. Conjunctivae are clear or only slightly erythematous. Treatment consists of cotton-tipped applicators dipped in diluted baby shampoo and applied to the base of the eyelashes. An antibiotic ointment (e.g., bacitracin, tobramycin, or erythromycin) may be applied to the lids at bedtime.

Other Ocular Emergencies and Trauma

Eye emergencies often first present by phone to the generalist. It is crucial that house officers recommend appropriate immediate care to the patient.

Eyes injured by splashed chemicals should be irrigated immediately for at least 30 minutes at the scene with water (sterile is preferable) before the patient is transported. If possible, patients should be transported with an eye shield to prevent further eye damage from rubbing the eye. Severe acid or alkali burns should be triaged to the emergency room after irrigation.

Blunt Eye Trauma

The physician should first take a complete history of the accident including exactly when it occurred, then observe the bony orbit for edema and hematoma, and gently palpate the orbital rim for irregularity indicating a step-off fracture. If a fracture is suspected, an orbital x-ray should be promptly ordered. The examiner should request the patient to open his eyelids to facilitate an inspection of the globe. An irregularity of the pupil should prompt suspicion of a ruptured globe. Do not touch the eye or eyelids if a ruptured globe is suspected. The examiner should evaluate for a limited range of ocular motion, which would alert the examiner to the likelihood of ocular muscle entrapment.

If a large *hyphema* (blood in the anterior chamber) is present, there may be an ocular emergency if the intraocular pressure is elevated (greater than 30 to 40 mmHg). Refer to the nearest hospital for ophthalmic consultation.

If the history of trauma seems unlikely or vague, or the details of the accident vary with repetitive questioning, the clinician should suspect abuse. The examiner should take a picture of the patient's injury and make detailed notes of their extent. If a child, the patient should be admitted to the hospital immediately, and full ophthalmic and physical examinations should be performed. Cases of suspected abuse should be reported to the proper au-

thorities. The presence of ruptured retinal vessels may indicate the “shaken baby syndrome” and is a cardinal sign of physical abuse.

Foreign Body

The examiner should evert the upper and lower lids to evaluate for the presence of a foreign body. When a foreign body is present on the cornea, or palpebral or bulbar conjunctiva, the patient may describe eye pain and exhibit tearing and increased blinking. If the practitioner is first contacted by phone, instruct the patient to refrain from rubbing his eye to prevent further corneal injury. The patient should be seen immediately in the medical office or referred to the emergency department for a slit lamp examination. After visual acuity testing and evaluation of the pupils, sterile water is used to wet the fluorescein strip of paper. The corneal defect will appear yellow/green when the blue Wood’s light illuminates the corneal surface. Vertical and linear “track mark” abrasions will likely indicate a foreign body on the palpebral conjunctiva of the upper lid. Once located, the foreign body should be removed with an eye spud. The eye may then be patched depending on the size and location of a corneal abrasion. If the wound does not appear healed within a 24- to 48-hour period, it should be evaluated by an eye specialist.

Iron-containing metallic foreign bodies in place for a few days can cause a substantial corneal rust ring that will deter normal reepithelization. If the physician is not accustomed to removal of rust rings with a rotating burr, referral to an ophthalmic practitioner is appropriate.

Lid Lacerations

These may be repaired by the generalist if only the skin is involved. Referral to a plastic surgeon or ophthalmologist is indicated if the tarsal plate is injured or for penetrating injuries involving the lids.

Penetrating Eye Injuries

These should be referred to an emergency room and an ophthalmologist for evaluation by CT scan to rule out foreign body remnants in the deeper structures. Patients should be transported with

the penetrating object in place without attempts to remove it in the field.

Visual Loss

Lesions *anterior* to the optic chiasm will affect only *one* eye. Lesions at the *chiasm* will affect *both* eyes partially (e.g., bitemporal hemianopsia). Lesions posterior to the chiasm will yield corresponding defects in both visual fields of the opposite side (homonymous hemianopsia or quadrantanopsia). Evaluation of the patient's visual fields should confirm the extent and nature of the field loss.

Transient Visual Loss. *Transient ischemic attacks* (either embolic or thrombotic) may lead to a sudden loss of vision. These are fairly common in older patients with systemic hypertension and/or valvular or ischemic heart disease. A thorough work-up should include a search for carotid bruits. A carotid duplex study should be ordered to exclude significant vascular disease and ulcerative plaque formation. In addition, an echocardiogram should be obtained to rule out the presence of valvular vegetations if substance abuse or mural thrombus is suspected.

Loss of vision associated with a tender temporal artery, fever, malaise, or painful mastication (jaw claudication) suggests temporal arteritis. A sedimentation rate would be strikingly elevated and collagen vascular panel is indicated (Chapter 27). If associated with polymyalgia rheumatism, the patient is at risk for blindness.

Giant cell arteritis requires immediate diagnosis and treatment if the nerve head is inflamed (papillitis). Decreased vision can be described as a curtain coming down over the upper visual field. The patient must be treated expeditiously with high-dose oral steroids (starting at 60 to 80 mg prednisone or equivalent/day) and tapered slowly over weeks to months, according to the patient's response.

Central retinal artery occlusion produces a sudden painless and marked unilateral visual loss and constitutes an ophthalmic emergency. The funduscopic exam shows a gray-white retina with a cherry-red colored fovea. Treatment by an ophthalmologist involves reducing intraocular pressure acutely (as with acetazolamide) in the hope that the arterial embolus will migrate distally, thus sparing more retina and having the patient breathe into a paper bag to increase blood CO₂ levels. The prognosis, even with immediate therapy, is extremely poor. An appropriate

work-up should include carotid duplex studies and on echocardiogram to exclude valvular or atrial thrombus, which could embolize to threaten the other eye.

Transient visual alteration lasting for seconds but recurring may be a sign of elevated intracranial pressure. The fundi should be carefully evaluated for papilledema. Pseudotumor cerebri is a frequent cause of papilledema, with patients complaining of headaches and visual disturbances. The causes are myriad but frequently include drugs such as vitamin A, tetracycline, naladixic acid, and birth control. The usual patient is female, overweight, and fertile.

An MRI or CT scan should be done before obtaining a spinal tap. If no abnormalities appear and the ventricles are small, an opening pressure greater than 200 suggests pseudotumor cerebri.

Transient visual changes may also occur in systemic disease such as poorly controlled *diabetes mellitus*. In brittle diabetic patients, the lens may become edematous and reduce visual acuity. Diabetic patients should be referred at the time of their initial diagnosis to an ophthalmologist for a baseline ocular evaluation. Refractive errors occur in diabetics due to the presence of increased glucose effecting a change in optical density. Such refractive errors should not be corrected until the diabetes is at its best stable level of control.

Ophthalmic migraine is discussed in Chapter 3.

Sudden Visual Loss. Patients may suddenly notice losses that have been present for long periods of time. Such awareness may occur as a patient looks through a microscope or telescope, or occludes one eye to watch an eclipse, having long adjusted to good unilateral vision. Examples of this phenomenon include *amblyopia* from childhood or congenital cataract. Causes of sudden true visual loss include central retinal vein or branch vein occlusions (“blood and thunder” fundus), optic neuropathy, papillitis, and retrobulbar neuritis. The latter is associated with pain on eye movement and occurs in multiple sclerosis.

Gradual Visual Loss. Gradual visual loss should be approached anatomically, proceeding from superficial and proximal to deep and posterior. One looks for changes in the cornea, lens media for cataracts, vitreous, or more posterior retinal problems such as *macular degeneration*.

Next, conditions affecting the nerve are considered. Tumors around the nerve such as *gliomas* or *meningiomas* can gradually

contract the field of vision. Processes at the chiasm such as *pituitary tumors* can cause loss of vision (superior temporal quadrantanopias). Tumors and intracranial processes usually respect the vertical midline, whereas in glaucoma, the defects respect the horizontal. CT or MRI studies can serve to localize the lesion more definitely.

Age-Directed Screening Examinations

The *newborn examination* is the generalist's opportunity to assess for birth trauma, birth-related eye infections, and to detect congenital syndromes. Pupillary constriction to light should be present after 32 weeks of gestational age.

The birth mother's chart should be reviewed for the presence of known sexually transmitted diseases. Silver nitrate ophthalmic drops, erythromycin ophthalmic ointment or tetracycline ophthalmic drops should be routinely instilled in the eyes of all newborns within 1 hour of birth to prevent chlamydial, gonorrheal, and other bacterial infections causing ophthalmia neonatorum conjunctivitis.

A single intramuscular dose of aqueous crystalline penicillin G (50,000 units) is used for term infants born to mothers with gonorrhea. However, conjunctivitis occurring after hospital discharge is presumed to be chlamydia, and the infant should be treated with a 10-day course of oral erythromycin to treat the conjunctivitis, and also to protect against potentially fatal chlamydial pneumonia.

In evaluating the cornea, the baby's head is elevated in the supine position, which will cause newborns to spontaneously open their eyes. A completely round red reflex should be present. Forceps delivery with compression of the globe may cause a rupture in Descemet's membrane, which has the appearance of black streaks in the red reflex. The ruptures are frequently curvilinear- or crescentic-shaped striae with possible overlying stromal opacification. Clearing of the cornea cloudiness normally follows endothelial and Descemet's membrane regeneration.

A white reflex may signify a congenital cataract, a retinal detachment, or tumor. If these conditions are found, a consultation with an ophthalmologist should be arranged. A dilated fundus examination should be done to rule out retinal abnormalities. Retinal hemorrhages secondary to the pressures re-

quired to mold the fetal head during transit through the birth canal are common in the neonate and usually resolve in several weeks.

Routine Eye Care and Screening

When an infant's birth weight is less than 1250 grams (2 pounds and 2 ounces), the infant should be referred to an ophthalmic practitioner to examine for the presence of *retinopathy of prematurity*.

1. In a well-baby visit, the infant's ability to fixate and follow a colorful and toy-like object should be evaluated. The Hirshberg reflex is used to evaluate binocular fixation by observing in central positioning of light source reflections in both pupils simultaneously. This procedure avoids the misleading presentation of large epicanthal folds creating the appearance of pseudostrabismus. Cover testing can demonstrate ocular misalignment by any movement of the habitually non-fixating eye upon forced fixation. These tests are appropriate for infants during the second half of the first year of life. For older toddlers, the addition of age-appropriate visual acuity charts can be helpful in determining adequate visual function.

Patients with suspected strabismus in which binocular fixation is not present should be referred for a timely evaluation. Strabismus and unequal refractive errors are common causes of amblyopia (i.e., reduced visual acuity not correctable by refractive means) in children. It is extremely important that these problems be accurately diagnosed and managed as early as possible while the visual system is still developing. This will assist in assuring that these infants have the best chance of attaining normal visual acuity in each eye. Amblyopia is discussed later in greater detail.

After the first month of life, *nasal lacrimal duct obstruction* is a major cause of conjunctival discharge. If pressure on the duct illicit a discharge, treatment should include massage of the duct, warm compresses, and topical antibiotics 4 times a day. The duct usually opens at or about 6 to 9 months. Referral for a nasal lacrimal duct probing is indicated if the obstruction does not open by 9 months or if the infection is so severe that it causes an orbital cellulitis.

2. Visual acuity of *preschoolers* can be tested with a picture chart or the illiterate E chart. They are generally able to cooperate with

a fundusoscopic examination using the direct ophthalmoscope to look for a normal disc and absence of retinal exudates. Nystagmus unexplained by seizure medicines should be investigated with CT scan or MRI.

3. All U.S. children attending school should have yearly visual acuity testing using the standard Snellen Chart at 20 feet to look for correctable problems such as myopia. Children with vision poorer than 20/30 should be referred to an optometrist or ophthalmologist.

Much controversy exists over the role of eye-care providers in learning disabled children. Visual training may be of benefit to some patients with specific problems but is not a panacea.

4. The true incidence of eye injury caused by sports is not known. A significant chance of injury is present in contact sports and games involving projectiles (badminton, squash, racquetball, handball, baseball, basketball, football, hockey, golf), as well as bicycling and in-line skating. The mechanisms of injury include laceration by sharp objects, blunt trauma to the eye (or orbit) and blow-out fractures of the bony orbit. Impact resistant polycarbonate glasses and goggles with or without a face mask should be recommended to reduce such injuries.

The *sports examination* should include visual acuity. Athletes with acuity less than 20/40 should be referred to an optometrist or ophthalmologist for corrective lenses before participation. If corrected vision is less than 20/100, the athlete should be informed of his increased risk for participation in sports. An injury to the sole sighted eye could lead to blindness. Those athletes wishing to participate despite this warning should use impact resistant lenses. Blind and partially sighted athletes should contact the U.S. Association for Blind Athletes for sports recommendations.

5. Adult eye screening should evaluate the eye as previously described. A history of occupational or hobby-related exposures should be taken. Industrial accidents involving the eye are relatively common. The retention of ocular foreign bodies occurs frequently in workers where grinding or soldering of metals takes place. Chemical exposure by splash or fumes can cause injury ranging from simple irritation to severe burns. The physician (and employer) should recommend polycarbonate lenses with side shields. Employers should provide eye wash stations and train employees in their immediate use.

6. The eye examination in *pregnancy* is important when pregnancy-related problems exist. Many manifestations of eye disease can occur in the patient with pregnancy-induced hypertension. The patient may report spots before her eyes. Findings include retinal hemorrhage, cotton wool spots, optic nerve ischemia (pale disc), and disc edema. Acute retinal changes are an indication for pre-term delivery.

Diabetic retinopathy during pregnancy may worsen rapidly and become irreversible if not treated aggressively. Insulin-dependent diabetics should be referred to their eye-care practitioner soon after the diagnosis of pregnancy. If proliferative changes are evident at the onset of pregnancy, the patient should be checked at intervals of 3 months or sooner, depending on the need for treatment.

7. The *geriatric* screening examination should document visual acuity. Referral for appropriate refraction is of the utmost importance to patient safety. Patients with substantial cataracts should be referred for possible therapy, including surgery. The retina is examined for tears, hemorrhages, cholesterol plaques, and hypertensive and atherosclerotic changes.
8. Screening patients with HIV infection should include a retinal examination at least twice yearly. This is especially important when the CD4⁺ T-lymphocyte count drops below 300/ μ L. Cytomegalovirus retinitis is the most common cause of vision loss in patients with HIV or AIDS and usually occurs when the CD4⁺ is less than 50/ μ L. The disorder presents as a granular, yellow-white retinitis, possibly with hemorrhage. Generally, treatment consists of ganciclovir, given first intravenously and then orally, or intravenous foscarnet.

Strabismus and Amblyopia

Amblyopia results from suppression of vision in one eye in situations of blockade of vision or diplopia at the crucial early stage of visual development. Strabismus, or malalignment of gaze, tending to produce diplopia, is noticed frequently in normal infants up to the age of 6 months. Prevalence of strabismus into adulthood approximates 4% of the population, half of whom (2%) suffer from suppression of the nonfixating eye, or *amblyopia*. Strabismus can be either exotropia or esotropia. Acquired strabismus may be accommodative or nonaccommodative. Accommodative strabismus results from attempts to accommodate to hyperopia,

particularly when it is unilateral (anisometropia), wherein concurrent over-convergence results in esotropia. To a lesser degree, gaze divergence may accompany unilateral myopia accompanying unsuccessful relaxation of accommodation for distance (exotropia). Diagnosing suppression or visual loss early can be crucial, particularly when caused by unilateral visual deprivation, such as in congenital cataract, blepharoptosis, corneal or vitreous opacity, hyphema, nonsupervised patching, or even prolonged use of atropine drops. Amblyopia resulting from intolerance of the diplopia that accompanies malalignment is generally reversible if treatment is started between the ages of 3 and 4 and irreversible if not corrected until after the age of 7.

Ocular Pharmacy

Patients should be instructed in the proper use of ophthalmic drops and ointments. When instilling ophthalmic drops, the patient should protect the sterility of the tip and of the bottle. The tip should be kept away from the lashes and fingers. After tipping the head back, the lower eyelid should be retracted inferiorly and the patient asked to fixate medially. The drop then can be placed gently into the lower cul-de-sac with minimal inconvenience to the patient. If the patient stares upward at the dropper, normal reflexes will cause the lids to occlude and some of the drop will be wasted. The lid will hold approximately half a drop. The patient should immediately be instructed to close the eyes and to move them in all directions to distribute the medicine over the ocular surface.

For installation of ophthalmic ointment, the lower lid is pinched to form a trough. A small ribbon of medicine can be applied without touching the tip of the tube to the lid, lashes or fingers. Use of ophthalmic ointments carries the disadvantage that vision becomes temporarily blurred while the ointment distributes over the cornea and until it is cleared by the tears. However, ointments often require less frequent application.

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Cardiovascular Problems

Chapter 5

Common Cardiac Problems in Ambulatory Practice

*Charles B. Eaton and
Anthony J. Cannistra*

CARDIAC MURMURS AND VALVULAR HEART DISEASE

Cardiac murmurs due to organic disease can generally be divided into those that occur because of the presence of abnormalities in cardiac structure, such as ventricular septal defect (VSD) or hypertrophic cardiomyopathy, and those which result from cardiac valvular pathology, such as aortic or mitral stenosis or regurgitation. These can be distinguished further by whether systolic or diastolic murmurs are present. Cardiac auscultation should be performed in a thorough fashion in a quiet room. Dynamic auscultation is also helpful to accentuate or diminish certain heart sounds so that accurate diagnosis can be made. Table 5.1 reviews

Table 5.1.
Heart murmurs.

Systolic					Diastolic				
	AS	MR	VSD	HCM	MVP	TR	AR	MS	
Timing	Sys: crescendo/ decrecendo	Holosystolic	Midpeaking pan-systolic	Sys: crescendo/ decrecendo	Mid, late or pan-systolic	Early to holosystolic	Diastolic: decrecendo	Diastolic: begins after OS (use diaphragm)	
Location	Base	Apex	LLSB 3–6th ICS	LLSB-apex	LLSB-apex	LLSB	Base, LLSB	Apex, very focal	
Neck	Pulsus parvus & tardus	Normal or collapsing	Small: normal mod. size: brisk	Rapid upstroke bisferiens	Normal	Increase JVP increase v-wave	Corrigan's	NI. or decreased volume	
Quality	Harsh	High-pitched, blowing	High-pitched, harsh	Harsh, associated MR	Honk, click, opening snap	High-pitched, blowing	High-pitched, blowing	Low, rumbling (use bell)	
Severity	Murmur/cartoid peak late	S3, CHF, cardiomegaly	Pulmonary HTN			Increase JVP, Longer hepatomegaly	Mur. starts earlier, ends later		
Diminish	Handgrip, inspiration, phase 2- valsalva	Inspiration, phase 2- valsalva	Phase 2- valsalva	Squat/supine/ handgrip/phase 4-valsalva	Squat/supine click/murmur later	Expiration	Standing/ inspiration	Inspiration	
Accentuate	Leg raise/squat/ phase 4-vals./ post-PVC	Squat/ handgrip	Handgrip	Phase 2- valsalva/stand/ post-PVC	Phase 2- valsalva/ stand click/ murmur earlier	Inspiration/leg raise	Squat/ handgrip/ lean forward	Exercise/cough/ handgrip, left lateral decubitus	

AS, Aortic Stenosis; MR, Mitral Regurgitation; VSD, Ventricular Septal Defect; HCM, Hypertrophic Cardiomyopathy; MVP, Mitral Valve Prolapse; TR, Tricuspid Regurgitation; AR, Aortic Regurgitation; MS, Mitral Stenosis.

Table 5.2.
Useful bedside maneuvers for dynamic cardiac auscultation.

Maneuver	Effect
Inspiration	Increases venous return
Expiration	Decreases venous return
Valsalva	Phase 1- intrathoracic pressure rises Phase 2- strain phase, decline in venous return Phase 3- abrupt decline in arterial pressure Phase 4- "over shoot phase," rise in arterial BP and reflex bradycardia
Handgrip	Transient rise in systemic vascular resistance (SVR), BP, HR, cardiac output
Squat	Increases venous return and SVR
Standing	Decreases venous return
Post-PVC	Increase in ventricular filling and contractility

the pertinent physical examination findings, and Table 5.2 lists some common dynamic bedside maneuvers that can be used.

Valvular Heart Disease-Aortic Valve

Aortic Stenosis (AS)

Aortic stenosis can be classified as congenital, rheumatic, or primary degenerative calcific AS (1). In general, patients who present with AS at age <30 years are likely have congenital AS, while those with a clinical onset between the ages of 30 to 60 years could have either congenital or rheumatic AS. Patients >60 years old are likely to have primary degenerative calcific AS. The underlying pathology differs depending upon the type of AS, with congenital and rheumatic disease involving fusion of the valve commissures, while primary degenerative calcific AS involves calcification of the valve leaflets. Bicuspid aortic valves are common in congenital AS, and calcification occurs as a secondary event in congenital and rheumatic AS. In addition, a patient with a suspected bicuspid aortic valve must be evaluated for coarctation of the aorta since this congenital defect also occurs in combination with bicuspid AS.

The hemodynamic consequence of AS is the limitation of cardiac output because of a fixed obstruction to left ventricular outflow caused by the stenotic valve. Left ventricular hypertrophy develops as compensation for the valvular obstruction, and thus, patients are often able to remain symptom-free for several years even in the presence of severe AS. However, survival decreases

with the onset of symptoms, and averages 3 years when angina or effort syncope occur, and 2 years with the development of congestive heart failure symptoms. The presence of CHF is ominous, since it reflects left ventricular dysfunction (2).

Diagnosis/Work-up. A history of angina, syncope, or dyspnea on exertion may be related to AS as well as to coronary artery disease and other causes. An EKG revealing LVH is a nonspecific finding.

Physical Examination. Classic aortic stenosis physical examination findings include diminished and delayed carotid impulses (pulsus parvus et tardus), a single S2, and a harsh mid- to late-peaking systolic murmur, best heard in the aortic area, but which can radiate throughout the precordium. The timing of the systolic murmur suggests the severity of AS, with an early peaking murmur signifying mild AS and a mid- to late-peaking murmur suggesting moderate to severe AS. A forceful point of maximal impulse (PMI) often indicates the presence of left ventricular hypertrophy. Caution must be taken when interpreting the carotid impulses in elderly individuals. Reduced vascular compliance occurs due to stiffening of the carotid arteries, and the “typical” parvus et tardus quality may be absent, even in the presence of significant aortic stenosis.

Diagnostic Tests. Cardiac echo examination is essential for the diagnosis and monitoring of aortic stenosis. Critical AS is defined as an aortic valve area of $<0.8 \text{ cm}^2$. Cardiac catheterization allows direct measurement of the pressure gradient across the aortic valve as well as accurate definition of the patient’s coronary anatomy. Aortic stenosis can be managed safely in an outpatient setting by establishing the diagnosis, then performing serial echocardiograms every 6 months to check for progression of stenosis severity. Exercise testing should not be performed when critical AS is suspected in a patient, since this can result in sudden death.

Treatment. Referral of a patient with AS is advised when symptoms, physical examination, and echocardiographic findings progress. Medications that can significantly alter both preload and afterload (e.g., nitrates, ACE inhibitors, calcium channel blockers), must be used judiciously or avoided. The heart cannot normally increase cardiac output in response to these changes due to the stenotic valve, and profound hypotension and cardiovascular collapse can develop. The mainstay of therapy is the surgical replacement of the stenotic valve with either a bioprosthetic or mechanical valve. Bacterial endocarditis prophylaxis both before and after surgery is also critically important (see Table 5.3

Table 5.3.
Endocarditis prophylaxis.

		Dosage for Adults	Dosage for Children ^a
Dental and Respiratory Procedures			
Oral			
Amoxicillin	3 gm 1 hour before procedure and 1.5 gm 6 hours later	50 mg/kg 1 hour before procedure and 25 mg/kg 6 hours later	
Penicillin allergy:			
Erythromycin	1 gm 2 hours before procedure and 500 mg 6 hours later	20 mg/kg 2 hours before procedure and 10 mg/kg 6 hours later	
Parenteral			
Ampicillin	2 gm IM or i.v. 30 minutes before procedure	50 mg/kg IM or i.v. 30 minutes before procedure	
<i>plus</i> Gentamicin	1.5 mg/kg IM or i.v. 30 minutes before procedure	2mg/kg IM or i.v. 30 minutes before procedure	
Penicillin allergy:			
Vancomycin	1 gram i.v. infused slowly over 1 hour, beginning 1 hour before procedure	20 mg/kg i.v. infused slowly over 1 hour beginning 1 hour before procedure	
Gastrointestinal and Genitourinary Procedures			
Oral			
Amoxicillin	3 gm 1 hour before procedure and 1.5 gm 6 hours later	50 mg/kg 1 hour before procedure and 25 mg/kg 6 hours later	
Parenteral			
Ampicillin	2 gm IM or i.v. 30 minutes before procedure	50 mg/kg IM or i.v. 30 minutes before procedure	
<i>plus</i> Gentamicin	1.5 mg/kg IM or i.v. 30 minutes before procedure	2 mg/kg IM or i.v. 30 minutes before procedure	
Penicillin allergy:			
Vancomycin	1 gram i.v. infused slowly over 1 hour beginning 1 hour before procedure	20 mg/kg i.v. infused slowly over 1 hour before procedure	
<i>plus</i> Gentamicin	1.5 mg/kg IM or i.v. 30 minutes before procedure	2 mg/kg IM or i.v. 30 minutes before procedure	

^aShould not exceed adult doses.

Adapted with permission from Medical Letter 1989; 313:112.

Table 5.4.

Common cardiac condition for which endocarditis prophylaxis is recommended.^a

Prosthetic cardiac valves, including bioprosthetic and homograft valves
 Previous bacterial endocarditis, even in the absence of heart disease
 Surgically constructed systemic-pulmonary shunts or conduits
 Most congenital cardiac malformations
 Rheumatic and other acquired valvular dysfunction, even after valvular surgery

Hypertrophic cardiomyopathy

Mitral valve prolapse with valvular regurgitation

Endocarditis prophylaxis not recommended

Isolated secundum atrial septal defect

Surgical repair without residua beyond 6 months of secundum atrial septal defect, ventricular septal defect, or patent ductus arteriosus

Previous coronary artery bypass graft surgery

Mitral valve prolapse without valvular regurgitation^b

Physiologic, functional, or innocent heart murmurs

Previous Kawasaki disease without valvular dysfunction

Previous rheumatic fever without valvular dysfunction

Cardiac pacemakers and implanted defibrillators

^aThis table lists selected conditions but is not meant to be all inclusive.

^bIndividuals who have a mitral valve prolapse associated with thickening and/or redundancy of the valve leaflets may be at increased risk for bacterial endocarditis, particularly men who are 45 years of age or older.

for recommended dosages and Table 5.4 for other cardiac indications for antibiotic prophylaxis).

Aortic Regurgitation (AR)

AR occurs most frequently on a rheumatic basis, but non-rheumatic causes include syphilis, myxomatous degeneration, bacterial endocarditis (particularly with bicuspid aortic valves), and connective tissue diseases such as Marfan's syndrome or ankylosing spondylitis. These conditions can result in either aortic valvular cusp distortion (endocarditis) or aortitis (syphilis, ankylosing spondylitis) leading to dilatation of the aortic root. Acute AR can also occur due to aneurysmal dissection involving the ascending aorta and the aortic valve.

Pathologically, left ventricular hypertrophy develops as an initial compensatory mechanism, and as AR progresses, LV function deteriorates due to increases in LV end-diastolic volume, pressure, and wall tension. As LV function worsens, the LV dilates and symptoms begin to occur. Patients with AR can remain asymptomatic

asymptomatic for several years, but when symptoms do develop, exertional dyspnea, orthopnea, and PND are the principal complaints. Anginal chest discomfort can also be a common complaint.

Physical Examination. The physical examination of chronic AR can be described by several classic signs. Severe, chronic AR produces a high-frequency, decrescendo diastolic murmur that can be best heard along the left or right sternal borders with the diaphragm of the stethoscope while the patient is sitting up, leaning forward, with the breath held in deep expiration (2). The severity of AR correlates with the duration of the murmur in diastole. A widened pulse pressure is also present in chronic AR. For further details, refer to Tables 5.1 and 5.2.

Diagnosis/Work-up. The assessment of AR should include baseline and repeated echocardiograms with Doppler to assess the anatomy of the aortic valve, the severity of the AR regurgitant jet, and to determine left ventricular size and contractility. In addition, serial exercise testing will provide important information about a patient's exercise tolerance. Cardiac catheterization is not necessary in mild or moderate AR, and should be performed when noninvasive testing suggests a worsening of LV size and function.

Treatment. Patients with mild to moderate AR and normal LV dimensions are usually asymptomatic for several years and require only careful clinical monitoring, serial echoes on a 6-month to yearly basis, and endocarditis prophylaxis. Patients with severe AR may also remain asymptomatic for several years, but usually require more frequent echocardiograms (every 3 to 6 months), and benefit from vasodilator therapy with agents such as ACE inhibitors or hydralazine aimed at reducing LV afterload. Digoxin and diuretic therapy are also useful in chronic compensated AR.

Valve replacement surgery should be deferred in asymptomatic individuals with normal LV function and recommended in symptomatic patients, even in the setting of preserved LV function. Thus, timing of aortic valve replacement surgery in asymptomatic patients with impaired LV function is controversial, signaled by increasing LV dimensions on echocardiogram after a long period without change. Every effort must be made to identify these patients before LV dysfunction deteriorates greatly, since LV impairment may become irreversible despite successful surgery, and long-term survival is reduced.

Mitral Regurgitation (MR)

The mitral valvular apparatus consists of the valve leaflets, mitral annulus, chordae tendinae, and the papillary muscles. Mitral regurgitation can result from a disruption in the structure or function in any of these four structural elements. Myxomatous degeneration and rheumatic heart disease account for the major etiologies of chronic MR, while endocarditis and myocardial ischemia, which results in papillary muscle dysfunction, are responsible for acute MR. MR results in increased left ventricular volume. It can remain asymptomatic for several years due to left ventricular compensatory dilatation. With further increases in LV volume, LV failure develops, and this event heralds the onset of progressive dyspnea, fatigue and exhaustion. Left atrial (LA) enlargement occurs due to the large regurgitant volume, leading often to atrial fibrillation.

Physical Examination. MR is characterized by a holosystolic murmur that is loudest at the apex and radiates to the axilla. Of interest, the intensity of the murmur is not proportional to the severity of MR. The PMI is displaced laterally because of LV enlargement, and with LA enlargement, the right ventricle can be displaced forward, resulting in a palpable RV lift. In advanced, decompensated MR, an audible S3 is present, and as left atrial pressure rises, pulmonary congestion develops. Left atrial enlargement and atrial fibrillation are frequent EKG findings.

Diagnosis/Treatment. Echocardiography is essential in the diagnosis and follow-up of MR. Left atrial and ventricular size and function are assessed, as well as the mitral valvular apparatus and the severity of MR. Medical management of the increased LV volume present in MR is achieved with afterload reduction therapy, diuretics, and digoxin, which enhances LV contractility and can also be beneficial in controlling the ventricular response if a patient is in atrial fibrillation. In addition, antibiotic prophylaxis is essential to prevent bacterial endocarditis (Tables 5.3 and 5.4).

Mitral valve surgery is associated with the highest operative mortality of all valvular surgery. A watchful eye on LV size and function is critical in deciding when to consider mitral valvular repair or replacement. If LV function begins to deteriorate, serious consideration for surgery must occur, even in asymptomatic patients, since LV dysfunction is associated with a higher opera-

five and long-term mortality. Cardiology consultation is advisable when serial echoes suggest a change in LV size and function. The consulting cardiologist can aid in the interpretation of these studies and facilitate other diagnostic testing, such as cardiac catheterization, which can provide direct hemodynamic measurements and further quantitate the severity of MR. Mitral valve repair (as opposed to replacement) for MR now has a great deal of appeal because the native valvular apparatus is preserved and operative mortality rates are lower.

Mitral Stenosis

Mitral stenosis (MS) occurs most frequently in patients who have a history of rheumatic heart disease. In this type, fusion of mitral valvular apparatus (commissures, cusps, chordae tendinae or combinations) results in mechanical obstruction of the mitral valve orifice (3). The normal mitral valve area is 4 to 6 cm² and critical MS occurs at areas ≤ 1 cm². As MS increases in severity, left atrial enlargement and atrial fibrillation occur because of increased LA pressure. Advanced MS is characterized by pulmonary hypertension and right heart failure.

Clinical History/Physical Examination. Rheumatic MS has a slowly progressive course over 10 to 20 years, and 2/3 of patients are females. The onset of symptoms occurs most frequently in the third and fourth decades of life. Exertional dyspnea is the most common symptom, but hemoptysis, chest pain, hoarseness (impingement of recurrent laryngeal nerve by enlarged left atrium), and thromboembolic disease are important clinical manifestations of MS. Left-sided (systemic) thromboembolism occurs in approximately 20% of patients with MS and 80% when atrial fibrillation exists. Patients with a dilated left atrium and low cardiac output are at a particularly high risk.

The characteristic auscultatory findings are listed in Table 5.1. The opening snap (OS) is a diastolic sound caused by the sudden tensing of the valve leaflets during opening and is best heard at the apex with the diaphragm of the stethoscope. The A2-OS interval is important to appreciate, since a shortening of this interval over time may indicate an increase in left atrial pressure, and thus, a worsening of MS. The OS may also decrease in intensity with worsening MS. The diastolic murmur of MS has a

low, rumbling quality, commences immediately after the OS, and is best heard through the bell of the stethoscope with the patient in the left lateral decubitus position. The duration of this murmur is directly correlated with the severity of the MS.

The EKG in these patients often demonstrates atrial fibrillation, left atrial enlargement, and with advanced MS, right ventricular hypertrophy (RVH). If left ventricular hypertrophy (LVH) is present, then coexistent valvular disease (MR, AS) should be considered. Finally, the chest radiograph may show characteristic straightening of the left heart border (left atrial enlargement), mitral annular calcification, cardiomegaly (RVH), and pulmonary vascular congestion.

Treatment. The medical management of MS is targeted at bacterial endocarditis prophylaxis (Table 5.3 and 5.4), the maintenance of normal sinus rhythm, rate control, and systemic anticoagulation if atrial fibrillation exists. The maintenance of sinus rhythm is desirable, since this preserves the important atrial contribution to left ventricular filling that normally occurs. This dependence increases with MS. If it is not possible to maintain sinus rhythm, agents such as digoxin, beta-blockers, or calcium channel blockers are useful to control rate.

Percutaneous or surgical management is appropriate to consider in three circumstances: the progression of symptoms despite adequate medical therapy, recurrent systemic emboli despite adequate anticoagulation, and the development of moderate pulmonary hypertension. The cardiac echo is an important tool to monitor the mobility of the valve leaflets, the amount of subvalvular thickening and calcification, and the left atrial size. With this information, a decision regarding the suitability of balloon mitral valvuloplasty to treat MS can be made by using now well-developed criteria (3).

The surgical treatment options include open valvular commissurotomy and valve repair or replacement. The decision on whether to choose percutaneous or surgical management is best made with the patient's age, lifestyle, and comorbid conditions in mind. For example, for a woman of child-bearing age with symptomatic MS, balloon mitral valvuloplasty may be the best choice (if other criteria are met) to enable her to have children and avoid the need for life-long anticoagulation, which would be necessary if the stenotic valve was replaced with a mechanical valve.

CORONARY HEART DISEASE

Epidemiology

Coronary heart disease is the leading cause of death in the United States. Each year nearly 500,000 deaths are caused by CHD, of which 80,000 occur in people under 65 years old. Each year approximately 1.25 million Americans suffer a myocardial infarction, and 300,000 have coronary artery bypass surgery. An estimated 7 million Americans have symptomatic CHD, accounting for 10 million office visits and more than 2 million admissions to the hospital. The estimated cost of care for CHD ranges from \$41.5 billion to \$56 billion per year (4).

CHD Risk Factors

While more than 200 risk factors for CHD have been studied, most coronary heart disease can be explained by age, family history, gender, cigarette smoking, elevated blood pressure, abnormal blood lipids, sedentary lifestyle, diabetes mellitus, and obesity. Table 5.5 lists each CHD risk factor, its prevalence, relative risk, and its population attributable risk. The population attributable risk reflects the burden of disease in the community, and calculates the theoretical percentage of the population that

Table 5.5.
Prevalence, relative risk and population attributable risk of risk factors for coronary heart disease.

Risk Factor	Prevalence	Relative Risk	Population Attributable Risk
Smoking	25%	3.5	38%
Sedentary lifestyle	78%	1.4	24%
Hypertension (BP >140/90)	30%	2.0	23%
Total cholesterol (>240 mg/dl)	27%	2.0	21%
Obesity (>130% IBW)	30%	1.4	11%
HDL cholesterol (<35 mg/dl)	11%	2.0	10%
Diabetes mellitus	6%	2.0	6%
Family history (First-degree relative younger than 55)	18%	3.0	Not modifiable

would be free of CHD if a particular risk factor were eliminated. Thus, from Table 5.5, if all of the population who smoked cigarettes stopped, we would expect a 38% reduction in the rate of CHD.

The details of the diagnosis and management of tobacco abuse, hypertension, diabetes mellitus, sedentary lifestyle, and obesity are covered in other chapters.

Coronary Artery Anatomy and Physiology

Two major coronary arterial trunks originate from the ascending aorta just after the aortic valve: the *right* coronary artery and the *left main* coronary artery.

Coronary vasculature can either be right or left *dominant*. In general, coronary artery dominance refers to the origin of the posterior descending (PDA) and atrioventricular nodal (AV) arteries. Therefore, although clearly the left anterior descending and left circumflex arteries supply the majority of the myocardium, most of the time, the PDA and AV nodal branches originate from the RCA, thus making the coronary vasculature *right dominant*. A right dominant circulation occurs in 85% of the population and refers to the situation in which the right coronary artery (RCA) follows the right AV groove and supplies blood to the right ventricular, as well as the inferior and posterior walls of the heart. In addition, two vital myocardial conduction components, the sinoatrial and atrioventricular nodes, receive their blood supply from the PDA branch of the RCA in a right dominant system.

The left main (LM) coronary artery in a right dominant coronary circulation gives rise to two major branch vessels referred to as the left anterior descending artery (LAD) and the left circumflex (LCx) artery. The LAD gives rise to septal perforator vessels, which supply the anterior interventricular septum, and diagonal vessels, which are responsible for supplying blood to the anterior and lateral walls of the heart. The distal LAD also supplies the distal anterior, as well as the apical aspect of the left ventricle.

A left dominant circulation occurs in approximately 8% of patients and refers to a situation in which the posterolateral left ventricular, posterior descending, and AV nodal arteries originate from the terminal portion of the left circumflex artery, while the RCA is nondominant, and supplies only a portion of the right atrium and ventricle.

Finally, approximately 7% of patients have a codominant or balanced system. This refers to the situation in which the RCA gives rise to the posterior descending artery, while the LCx artery supplies the posterolateral left ventricular artery.

The issue of coronary circulation dominance may be critically important in decisions involving coronary revascularization strategies. For example, stenosis in the RCA in a left dominant system may not be clinically relevant, and medical management alone may be the best treatment option. A stenosis in the proximal portion of a LCx vessel in a left dominant coronary artery system, however, translates into a large area of myocardium at risk for ischemic damage and may support an aggressive revascularization strategy. Significant obstructive coronary artery stenoses occurring in the LAD vessel are usually clinically important and deserve an appropriately aggressive treatment approach regardless of the patient's coronary artery system dominance. The issue of left main coronary artery stenosis deserves special mention. The presence of significant left main coronary artery disease is usually associated with symptoms of angina pectoris, and medical management in stenoses $>60\%$ have an unfavorable prognosis. This mortality risk increases even further in left dominant system. Therefore, once left main disease is diagnosed, urgent or emergent coronary artery bypass grafting surgery should be considered, since this confers the greatest survival advantage to the patient. In general, a stenosis is considered to be hemodynamically significant if it occupies $>70\%$ of a blood vessel's luminal diameter measured during cardiac catheterization.

Clinical Presentation and Natural History of CHD

Coronary heart disease may be asymptomatic, present with symptoms of chest pain, syncope, dyspnea on exertion, palpitations, heart attack or sudden death. At least one-fourth of the nearly 1 million first heart attacks per year result in death within a few hours, which is one of the reasons why prevention is so important. No matter what the presentation of coronary heart disease, its long-term prognosis is related to the number of vessels affected and the degree of left ventricular functional impairment.

Angina pectoris is a symptom complex of substernal chest pain or pressure associated with exertion and relieved by rest.

The frequency of angina and the severity of pain are not related to the degree of coronary atherosclerosis or prognosis except for pain at rest. Unstable angina, however, defined as a changing pattern of exertional angina and angina at rest has a worse prognosis. Stable and unstable angina are the initial manifestation of CHD in 65% of women and 40% of men under age 65. Approximately 12% of patients with unstable angina will have a myocardial infarction within 2 years of diagnosis.

Acute myocardial infarction or irreversible myocardial damage as the result of prolonged ischemia remains the most common presentation of coronary heart disease in the United States. The typical presentation includes a history of greater than 30 minutes of crushing chest pain, usually the most severe in the patient's life, associated with radiation to the jaw or arm, accompanied by nausea, vomiting, diaphoresis, diarrhea, or faintness. The short- and long-term survival is variable. Complications of pump failure, infarct extension, papillary muscle rupture, septal rupture, ventricular aneurysm, dysrhythmias, and conduction blocks may occur. Non-Q MI or subendocardial MI has a lower in-hospital case-fatality rate compared with transmural MI, but the same long-term survival. Nontransmural infarcts have a higher risk of extension and reinfarction rate and should perhaps be considered as incomplete events. Whether aggressive interventional therapy will change these former trends remains to be tested.

Silent MI or an unrecognized infarct found after the fact by EKG carries a worse prognosis than a disease-free cohort but much better than a patient with recognized myocardial infarction. It appears to be more common in women, older men, and perhaps diabetics. It is associated with age, cigarette smoking, hypertension, LVH, and peripheral vascular disease but not lipid abnormalities and psychosocial factors.

Sudden cardiac death or death within 1 hour of onset of symptoms occurs in 20% to 25% of patients who present with CHD. It is the most prevalent form of CHD excluding hospital patients. In 80% of cases, it is sudden without prodromal symptoms. Death occurs presumably due to ventricular fibrillation, with patients usually having severe pre-existing coronary atherosclerosis on autopsy. Among patients who are resuscitated from an out-of-hospital arrest, many are left with significant sequelae and 25% to 50% die within 4 years.

Diagnostic Testing to Detect Coronary Heart Disease

Noninvasive Tests

Exercise Treadmill Testing. The reasons to perform exercise treadmill testing are to aid in the diagnosis of coronary artery disease, to establish the presence of ischemia after myocardial infarction, to estimate prognosis after myocardial infarction, and to determine a patient's functional capacity. A patient's response to exercise is evaluated by observing the duration of exercise, heart rate response to exercise, blood pressure response to exercise, angina during exercise and electrocardiographic ST segment changes induced during exercise. Table 5.6 lists exercise testing results associated with adverse patient prognosis, multivessel, or left main coronary artery disease. Contraindications to exercise treadmill testing are unstable angina, aortic stenosis, and hypertrophic cardiomyopathy.

Radionucleotide Scanning. The three most common reasons for choosing alternative stress testing are increased diagnostic sensitivity and specificity compared with regular treadmill testing, an abnormal baseline EKG (e.g., ST-T wave abnormalities, left ventricular hypertrophy, left bundle branch block) and patient physical limitation (e.g., severe peripheral vascular disease, neurological impairment involving lower limbs).

Radionuclide agents combined with treadmill testing are necessary to evaluate patients with certain abnormal baseline ECGs. Thallium 201 and technetium Tc 99 m labeled sestamibi are the most commonly used radioisotopes to help to diagnose

Table 5.6.
Exercise parameters associated with an adverse prognosis and multivessel coronary artery disease.

Duration of symptom-limiting exercise
Failure to increase systolic blood pressure ≥ 120 mm Hg, or a sustained decrease ≥ 10 mm Hg, or below rest levels, during progressive exercise
ST-segment depression ≥ 2 mm, downsloping ST segment, starting early in exercise, involving ≥ 5 leads, persisting ≥ 5 minutes into recovery
Exercise-induced ST-segment elevation (a VR excluded)
Angina pectoris during exercise
Reproducible sustained (>30 sec) or symptomatic ventricular tachycardia

Adapted with permission from Braunwald E. Heart disease, a textbook of cardiovascular medicine. 4th ed. Philadelphia: WB Saunders, 1992:168.

the presence of elicitable, reversible myocardial ischemia. Radionuclide images are now typically obtained using single photon emission computer tomography (SPECT), which further enhances sensitivity.

In patients who are unable to exercise, pharmacological agents such as dipyridamole, adenosine, and dobutamine can be used with either thallium or sestamibi to evaluate the possibility of elicitable myocardial ischemia. Pharmacological stress testing with either dipyridamole or adenosine is contraindicated in patients with severe reactive airway disease, since it may provoke bronchospasm. In this situation, pharmacological stress testing using dobutamine should be considered. Dobutamine increases heart rate, blood pressure, and myocardial contractility, and thus, can produce ischemia similar to actual exercise treadmill testing.

Stress echocardiography is a noninvasive test growing in popularity for diagnosis of coronary heart disease. Cardiac echocardiography can be combined with either treadmill or pharmacological stress testing. The sensitivity and specificity of stress echo compare favorably with other imaging modalities. This technique is dependent upon the skill level of the operator and the body habits of the patient. In general, adequate echocardiographic images in overweight individuals are more difficult to obtain. Dobutamine echocardiography has advantages over stress echo, which requires that images be obtained immediately after exercise when respiratory artifact is greatest, making image acquisition more difficult.

Invasive Diagnostic Tests. *Cardiac catheterization* is the most commonly used technique to invasively diagnose and evaluate coronary artery disease. A variety of intracoronary diagnostic modalities are also available and are currently used mostly for investigational purposes. Examples include coronary angiography and intravascular ultrasound. Coronary angiography permits visualization of the coronary artery endothelial surfaces. Intravascular ultrasound permits direct measurement of coronary vessel size, wall thickness and internal lumen diameter.

The primary goal of *coronary angiography* is to define the anatomy of the coronary circulation in patients with known or suspected coronary artery disease and to use this information to aid in future patient management. Common indications for coronary angiography include new onset angina, unstable angina, evaluation before a major surgical procedure, silent ischemia,

atypical chest pain, acute myocardial infarction, postinfarction angina, and failed thrombolysis.

Contraindications for cardiac catheterization include uncontrolled congestive heart failure, high blood pressure, dysrhythmias, recent cerebrovascular accident (<1 month), active infection, electrolyte imbalance, acute renal failure, acute gastrointestinal bleeding or anemia, pregnancy, anticoagulation (or known, uncontrolled bleeding diathesis), uncooperative patient, and medication intoxication (e.g., digitalis, phenothiazine).

It should be noted that all indications and contraindications of diagnostic cardiac catheterization should be considered relative and based on the condition and safety of individual patients. The major complications associated with cardiac catheterization procedures are death, myocardial infarction, stroke, dysrhythmia, vascular injury, contrast reaction, cardiac perforation, or tamponade. Each complication occurs with a frequency of 1:1000. Complications rates are greater in patients over age 60, with multivessel disease or left main disease, with reduced ejection fractions ($EF < 30\%$), those who often have the strongest indications of angiography.

Treatment

Medical Therapy. In preventing progression of atherosclerosis, lipid lowering therapy has been shown to reduce recurrent MI and cardiac death by 35%. Smoking cessation lowers risk of recurrent MI by 50%. Blood pressure control has a more modest benefit in reducing CHD mortality.

Preventing pathologic thrombosis by prescribing aspirin, coumadin, or Ticlid reduces the risk of recurrent myocardial infarction by 25% to 34%. Preventing ischemia using long- and short-acting nitrates relieves the symptoms of angina although it has little benefit in improving mortality. Beta blockers both improve control of anginal symptoms and are associated with reduced mortality in postmyocardial infarction patients. Calcium channel blockers reduce symptoms in patients with angina and variant angina but have not improved mortality. Preventing ventricular dysrhythmias through use of medications has been difficult to perform and has not been effective therapy. Implantable defibrillators have improved survival in patients with symptomatic recurrent ventricular tachycardia or fibrillation. Preventing left ventricular dysfunction with the use of angiotensin converting

enzyme inhibitors has reduced the risk of recurrent MI and sudden death in postmyocardial infarction patients with reduced ejection fraction ($EF < 40\%$). Ongoing trials will help determine whether it is helpful in post-MI patients with normal ejection fractions.

Invasive Therapy. Percutaneous transluminal angioplasty (PCTA), atherectomy, intracoronary stents, or coronary artery bypass grafting surgery may be performed electively, urgently, or on an emergency basis. Electively, the most common indication for invasive therapy is failed medical management, with the patient having persistent symptoms of ischemia. If the patient has multivessel coronary disease or left main disease, then coronary artery bypass graft surgery is indicated, since it not only relieves symptoms but enhances survival. Otherwise, if the patient has a symptomatic coronary artery stenosis greater than 70% despite an adequate trial of medical management, then PCTA is usually recommended. Urgent indications for invasive therapy are unstable angina after an infarction, a large area of myocardium at risk, e.g., proximal LAD lesion, renewed symptoms after attempted angioplasty (probable restenosis), symptomatic obstructive coronary disease, and concomitant valvular heart disease. Emergency indications include failed thrombolysis, shock, mechanical complications such as ruptured papillary muscle, ventricular septal defect, or aortic dissection.

After invasive therapy, patients need close monitoring not only for evidence of renewed symptoms, but for aggressive medical management of risk factors.

◀ Congestive Heart Failure (CHF)

Epidemiology. Unlike cardiovascular disease, the incidence and prevalence of CHF has been increasing in the last 2 decades, especially in the elderly. Nearly 4 million Americans have CHF, and 400,000 new patients develop heart failure on a yearly basis. By age 75, nearly 10% of the population has CHF. Severe CHF carries a 5-year survival rate of 50%, which is worse than for most forms of cancer. With advances in management (the addition of ACE inhibitors), the average mortality is slowly improving. Recent Framingham Heart Study data suggest that hypertension and myocardial infarction contribute the highest population attributable risk for congestive heart failure, with hypertension accounting for 39% of male patients and 59% of female patients.

Myocardial infarction accounts for 34% of male patients but only 9% of female patients. Therefore, early and aggressive therapies to control blood pressure offer promise in reducing the incidence of CHF and its associated mortality.

Pathophysiology. Congestive heart failure is defined as a disease characterized by clinical evidence of systemic venous or pulmonary congestion at rest or with exercise that results from an abnormality in the systolic and/or diastolic performance of the heart. Systolic dysfunction is characterized by reduced ejection fraction, reduced contractility, and left ventricular dilation. Neurohumoral adaptations include activation of the renin-angiotensin system, increased catecholamine discharge, and increased atrial natriuretic peptide release that leads initially to increased cardiac output through the Frank-Starling mechanism, but at the expense of increased preload (end diastolic filling pressures) and increased afterload (resistance to ejection of blood). More often diastolic dysfunction becomes apparent when hearts with systolic dysfunction reach their limit of dilation and resistance to diastolic filling increases. Pure diastolic dysfunction without systolic dysfunction can occur, but this is uncommon and generally involves extensive left ventricular hypertrophy such as found in idiopathic hypertrophic subaortic stenosis (IHSS), hypertension or aortic stenosis. In addition pure diastolic dysfunction is associated with subendocardial disease, or infiltrative myocardial disease.

Clinical Presentation. Most CHF develops insidiously, with the patient developing right (JVD, hepatomegaly, and peripheral edema) and left heart failure (orthopnea, dyspnea, rales), in a low output state (cool, vasoconstricted extremities) in a patient with both systolic and diastolic dysfunctions. Classic symptoms and signs are leg edema, orthopnea, paroxysmal nocturnal dyspnea (PND), rales, and jugular venous distention (JVD). Congestive heart failure, however, may either present abruptly as in acute pulmonary edema, and be associated with a high output state (warm, flushed extremities), or present only with right heart symptoms and only with diastolic dysfunction.

History and Physical Examination. The history and physical examination should document evidence of left heart failure, such as dyspnea on minimal exertion, nocturnal cough, tachycardia, paroxysmal nocturnal dyspnea, or right heart failure such as JVD, hepatomegaly, or bilateral ankle swelling. The history should

then focus on defining the etiology of CHF, such as the nature of any pre-existing heart disease such as coronary ischemia, hypertension, or valvular heart disease. Evidence of reversible causes such as salt intake or alcoholic cardiomyopathy, substance abuse (cocaine) or infection should be investigated. The physical examination should document signs of left and right heart failure, such as neck vein distention, pulmonary rales, S3 gallop, hepatojugular reflex, hepatomegaly, pleural effusions, and baseline tachycardia.

Laboratory evaluation should include a CBC to rule out anemia, electrolytes, BUN, creatinine, liver function tests, phosphate, magnesium, and urinalysis. A chest x-ray is indicated to evaluate cardiac size and pulmonary venous congestion. An electrocardiogram allows evaluation of chamber enlargement and myocardial ischemia.

Assessment of left ventricular function with an echocardiogram is indicated on all patients. If a poor acoustic window is present, then a radionucleotide gated study is indicated. If the ejection fraction is found to be greater than 40%, then diastolic dysfunction should be considered. Doppler echo usually allows for evaluation of diastolic dysfunction at the level of the mitral valve. An echocardiogram also allows for evaluation of valvular disease, and akinetic or hypokinetic areas may represent evidence of damaged myocardium from coronary heart disease.

Therapy is focused on correcting any underlying reversible process, such as myocardial ischemia, hypertension, valvular heart disease, cardiomyopathies. One must determine the etiology of the heart failure and not treat just the symptoms.

ACE inhibitors, diuretics, and digitalis are the cornerstones of pharmacologic therapy for CHF. ACE inhibitors are the drugs of choice for patients with systolic dysfunction, favorably reducing both preload and afterload. Several trials have convincingly shown that ACE inhibitors not only control symptoms of CHF but also improve mortality. Diuretics are important initial therapy when fluid overload is evident. Several recent controlled trials have shown that patients with mild to moderate CHF did better acutely on diuretic therapy alone than on ACE inhibitors alone, but diuretics alone did not improve long-term outcomes as much as ACE inhibitors. While diuretics improve the symptoms of peripheral edema and pulmonary venous congestion, they stimulate the counter regulatory neurohumeral mechanisms of the

renin-angiotensin system and systemic catecholamines, leading to increased afterload and further sodium retention. The combination of ACE inhibitors and diuretics together prevents these maladaptive compensatory mechanisms.

Digitalis still plays a role in treating patients with enlarged hearts, an audible S3 gallop, and an ejection fraction of less than 40%. It is the only standard pharmacologic therapy that increases contractility and may have a beneficial effect on the counterregulatory neurohumoral mechanisms alluded to previously. Digoxin is indicated in patients with rapid atrial fibrillation and CHF or in patients with uncontrolled hypertension or critical aortic stenosis and CHF. Digitalis is contraindicated in patients with hypokalemia and myocardial ischemia, and in patients with hypertrophic cardiomyopathies or significant diastolic dysfunction. In patients with *diastolic dysfunction*, calcium channel blockers are the treatment of choice. They have anti-ischemic actions, preload reduction, blood pressure control, LVH regression potential, and heart rate control, which leads to increased coronary filling during prolonged diastolic relaxation. Beta-blockers that control heart rate may also be helpful therapy for pure diastolic dysfunction.

Nonpharmacologic therapy is also important. Avoid beta-blockers (even ophthalmic preparations, if possible) and calcium channel blockers in patients with *systolic dysfunction* because they are myocardial suppressants. Nonsteroidal anti-inflammatories such as indomethacin may worsen severe CHF patients with active renin-angiotensin systems and hyponatremia. Alcohol should be restricted if an alcoholic cardiomyopathy is suspected. A no-added salt diet is helpful in reducing the dosage of diuretic needed. Activity prescription should be individualized to minimize excessive myocardial work while maintaining the patient's functional capacity. Supervised exercise programs in cardiac rehabilitation are particularly helpful in increasing a patient's exercise capacity.

Supraventricular Dysrhythmia

Atrial Fibrillation (AF). This common dysrhythmia occurs in up to 4% of patients over 60 years of age (5), and may be either chronic (associated with organic heart disease) or paroxysmal. In AF, normal contraction of the atria is lost, and rapid and chaotic

stimuli of the atrioventricular node (AV) occur. Electrocardiographically, this is reflected in the absence of P-waves and a ventricular response that is rapid and irregular. Coarse fibrillatory waves are most noticeable in lead V_1 of the EKG. Chronic AF is usually associated with hypertensive, ischemic, valvular, cardiomyopathic, or pericardial heart disease. Paroxysmal AF can occur in normal individuals (lone atrial fibrillation), and with conditions such as sick sinus syndrome, the Wolff-Parkinson-White (WPW) syndrome, or organic heart disease. In addition, comorbid conditions such as hyperthyroidism or activities such as alcohol use or abuse are known precipitants of paroxysmal AF.

In an office setting, once the history, physical examination and EKG are obtained, the main priority is to control the ventricular response (VR) to ensure hemodynamic stability. Immediate hospital admission should occur if the patient is hemodynamically compromised or symptomatic. If the patient is stable and asymptomatic (VR~90 to 110 beats per minute), then outpatient rate control measures with agents such as digoxin, beta or calcium blocking agents can be considered. A low threshold to admit the patient to the hospital is necessary for rates ≥ 110 and if other conflicting medical conditions (chronic renal failure) or concern about patient compliance exists. If the ventricular response is ≤ 80 beats per minute (bpm), then AV blocking agents should be avoided. Otherwise, beta-blockers, in the absence of any contraindication, are extremely effective rate controlling agents, since they control sympathetic tone by blocking the effect of catecholamines on beta-adrenergic receptors. Digoxin may be particularly useful when left ventricular dysfunction exists.

Once rate control is established, efforts should be geared toward the conversion of AF back to normal sinus rhythm. At this time, cardiology consultation is encouraged to determine when this should occur. It is recommended that anticoagulation therapy should be started if the AF is >2 days (6), since cardioversion is associated with cerebral and systemic emboli. Transesophageal echocardiography (TEE) is used increasingly to help in this decision, and a cardiology consultant can offer suggestions regarding this technology. Otherwise, a transthoracic echo provides important information about left atrial size as well as left ventricular function. It becomes increasingly difficult to convert AF and to maintain sinus rhythm with increasing left atrial size (>4.0 mm). Cardioversion can occur by either electrical or chemical means. Chemical cardioversion requires short-term hospital admission

to monitor for the presence of proarrhythmic effects from the agents such as quinidine or procainamide.

Once cardioversion has been attempted and is successful, the patient can be followed on an outpatient basis. Anticoagulation should occur for 4 to 6 weeks after cardioversion, since atrial stasis and, therefore, atrial thrombus formation, can occur during this period of time. If cardioversion is unsuccessful, then efforts to control the ventricular response and to initiate long-term anticoagulation are appropriate.

Two circumstances bear special attention. AF that occurs in a patient with the WPW syndrome can conduct rapidly down the bypass tract (>180 bpm) and create profound hemodynamic compromise. These episodes are usually well tolerated and brief, but if they are frequent and prolonged, require urgent admission to the hospital and cardioversion, since this dysrhythmia can quickly degenerate into ventricular fibrillation. In this situation, AV nodal blocking agents such as digoxin, beta, and calcium blockers are contraindicated, since blocking the AV node can preferentially cause increased conduction down the bypass tract.

Multifocal Atrial Tachycardia (MAT). MAT is defined electrocardiographically as a rhythm with three different P-wave morphologies occurring at rates >100 bpm. If rates are <100 bpm, the term wandering atrial pacemaker is used. These rhythms can appear irregular and thus, mimic AF. Atrial rates are usually not as fast as in acute AF, and these dysrhythmias are commonly seen in patients with preexisting pulmonary disease.

Atrial Flutter. The diagnosis and management of atrial flutter is similar in many respects to atrial fibrillation. In atrial flutter, atrial contraction is rapid at rates of 280 to 300 bpm with variable AV block. This results in ventricular response rates of 70 to 150 bpm. In addition, regular sawtooth patterns of atrial contractions can be seen on EKG (especially lead VI). Carotid sinus massage (CSM) performed in the proper clinical setting can be useful to display flutter waves if they are not readily apparent on EKG without blockade. A combination of atrial fibrillation and flutter is common.

Paroxysmal Supraventricular Tachycardia (PSVT). PSVT occurs because of sustained reentry mechanisms involving the sinoatrial node (SA-node), atrium, and AV node. In general, this dysrhythmia can take the form of either a paroxysmal atrial tachycardia with block (PAT) or an AV nodal reentry tachycardia

(AVNRT). Again, CSM is useful to differentiate these two types of dysrhythmias. Paroxysmal atrial tachycardias are not affected by vagal stimulation, although enhanced AV block may occur. This is usually manifested by progressive PR prolongation on EKG. For AVNRT vagal maneuvers either have no effect on the tachycardia or cause it to terminate. For PAT and AVNRT, it is important to search carefully for the presence of atrial activity and to determine the rate of the atrial complexes. For reentry circuits involving the AV node, a common finding is that of retrograde P-waves seen "buried" in the ST-T wave portion after the QRS complexes on the EKG. PAT with block is a dysrhythmia commonly found in a patient who may have digoxin toxicity, and this state should be ruled out if PAT with block is diagnosed.

Ventricular Tachyarrhythmias. Ventricular tachyarrhythmias usually occur in the setting of advanced organic heart disease such as acute or old myocardial infarction and congestive heart failure. An important goal of family medicine physicians is to identify those patients who are at highest risk for the development of life-threatening dysrhythmias and to participate in the management of these individuals in a concerted effort with cardiology consultants. The presence or absence of symptoms determines how aggressively a particular dysrhythmia should be managed.

Unifocal ventricular premature beats (VPBs) can have either a right or left bundle branch morphology on EKG. VPBs are common and can occur in patients with and without underlying heart disease. The vast majority of VPBs are associated with minimal or no symptoms and do not need to be treated with specific antiarrhythmic medication. In fact, antiarrhythmic medication may itself be proarrhythmic and thus, should be avoided in these patients. A thorough review of medications (e.g., digoxin, diuretics) and directed lab testing to include potassium, magnesium, and phosphorus should be considered.

The EKG characteristics commonly associated with ventricular tachycardia (VT) include wide, bizarre QRS complexes (0.14 to 0.16 seconds); AV dissociation; positive QRS complexes in all of the precordial leads (lead concordance), and capture or fusion beats. It is worth mentioning that wide complex tachycardias (WCT) are not always ventricular in origin. The differential diagnosis of WCT includes all of the supraventricular tachyarrhythmias listed above. In addition, if these SVTs are conducted aberrantly, or occur in the presence of a preexisting left or right

undle branch block, they can appear as wide. Lastly, antegrade conduction through a bypass tract in a patient with WPW can have wide appearance. If possible, it is useful to examine the onset of the tachycardia. For example, if the tachycardia begins after a premature atrial contraction, it is likely to be supraventricular, but if it begins after a premature ventricular contraction, then it may be either junctional or ventricular in origin.

Nonsustained or sustained ventricular tachycardia is much more worrisome than isolated VPBs, especially when these dysrhythmias occur in the setting of left ventricular dysfunction. These dysrhythmias frequently occur in the postmyocardial infarction setting, but specific therapy should be reserved for individuals who are symptomatic (i.e., syncope, out-of-hospital cardiac arrest).

Specific diagnostic therapeutic strategies need to be individualized for each clinical setting. An assessment of left ventricular function with cardiac echo or diagnostic cardiac catheterization is imperative. Ambulatory Holter monitoring can be helpful to determine the frequency of symptomatic ventricular dysrhythmia. Exercise testing can be used to determine whether ventricular dysrhythmia is inducible. This type of testing can also be useful to assess the efficacy of medical therapy.

The use and results of electrophysiologic study (EPS) are controversial, but many cardiologists prefer to have selected patients undergo this type of invasive testing to help define the VT and guide drug selection for symptomatic dysrhythmia suppression. Some forms of VT induced on EPS cannot be suppressed with drug therapy. In this situation, consideration must be given to the insertion of an automatic implantable cardioverter defibrillator (AICD). AICDs may also be useful in patients on adequate antiarrhythmic therapy who sustain an out-of-hospital cardiac arrest. The details of EPS are beyond the scope of this chapter.

Bradyarrhythmias. Bradyarrhythmias cover a broad range including sinus bradycardia (rate <60 bpm), sinoatrial block, sinus arrest, and conduction disturbances such as first-, second- or third-degree heart block. These disturbances most often occur in the setting of underlying cardiac disease. A thorough review of a patient's medications will often reveal agents that may be contributing to the occurrence of advanced degrees of heart block. Removing the inciting agent will often abolish the severity of the conduction system disease. However, if the process results in

symptoms, cardiology consultation and consideration for permanent transvenous pacemaker therapy is appropriate. If possible, a dual-chamber pacemaker, which can sense and pace both the atria and ventricles, is preferable to maintain AV synchrony.

The sick sinus syndrome (SSS) can be a clinically important process. On EKG, the SSS can present in several ways, including severe sinus bradycardia, sinus arrest, sinoatrial block, bradycardia alternating with tachycardia, and AF with failure of resumption of sinus rhythm after cardioversion. It is a common cause of syncope, especially in the elderly population, and can be diagnosed on ambulatory outpatient or inpatient telemetry monitoring. If present, a permanent transvenous pacemaker is indicated for treatment.

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Peripheral Vascular Disease

Kurt Kurowski

ACUTE ARTERIAL OCCLUSION

The predominant cause of acute occlusion is embolism, the overall incidence of which is estimated at 0.05% of hospital admissions (1). Ninety percent of peripheral embolism originates from the cardiac chambers, but it may occur from vessel aneurysms or even from distal embolization of atheromatous plaque within branches of the arterial system. The most common underlying cardiac abnormality is atrial fibrillation, followed by myocardial infarction, the latter surpassing rheumatic heart disease as a source for emboli. The risk of embolization in myocardial infarction is greater with a larger, transmural, or anterior wall infarction. The risk in atrial fibrillation increases with alternation between sinus rhythm and atrial fibrillation and with enlargement of the left atrium associated with mitral stenosis. The incidence of systemic embolization in patients with atrial fibrillation and mitral stenosis is 25% to 30% (2), compared with 5% to 10% in mitral stenosis without atrial fibrillation. Five percent of patients in the acute phase after myocardial infarction have peripheral arterial emboli. Because of the relatively large incidence of myocardial infarction, this accounts for about 30% of all emboli seen (3).

Thrombosis of the peripheral arteries appears to be less common than embolism by a ratio of 1:4 (4). Patients with acute thrombosis usually have evidence of chronic atherosclerosis affecting their coronary and/or peripheral circulation, and in

sharp contrast with patients with embolism, they rarely have atrial fibrillation.

Pathophysiology

In most common situations, thrombosis occurs in arterial vessels already partially occluded by arteriosclerosis and/or ulcerated plaque. Anything that significantly impedes the arterial blood flow may predispose to the actual thrombotic event. This includes heart failure, severe dehydration, a significant elevation in the hematocrit (such as in polycythemia), an inflammatory arteritis, or trauma to the arterial intima, such as from repetitive arterial punctures or canalization procedures, or even continuous external compression of an artery, such as is seen in thoracic outlet syndrome.

Clinical Presentation

History

Patients complain of pain and coldness in the limb distal to the site of occlusion. A sense of numbness or paresthesias over the involved portion of the extremity is frequently reported. Symptoms develop fairly rapidly (over a period of minutes to hours), and gangrenous changes may develop in the involved extremity, depending on the degree and site of the occlusion and the state of any collateral circulation. Patients with thrombosis, as opposed to embolization, are more likely to have symptoms and risk factors suggesting chronic underlying arteriosclerosis of other arteries as well.

Physical Examination

Earliest physical evidence of acute occlusion is a cold extremity with no palpable pulses distal to the site of occlusion. A pallor is usually seen in the affected limb, and it becomes worse with elevation. Later stages feature blister formation progressing to gangrene in the distal aspects of the affected limb.

Diagnostic Studies

Arteriography is recommended to establish the site and degree of occlusion as well as to evaluate the status of any collateral circulation. Magnetic resonance angiography may be substituted, particularly in those patients with a history of contrast dye allergy.

Patient Management

Trauma to the skin of the affected extremity must be avoided. The patient is usually placed on a heparin drip to maintain PTT 1.5 to 2.5 times control value after receiving a 5000 unit heparin bolus.

Patients with emboli are best treated with urgent embolectomy if no evidence of ischemic necrosis appears, and if no more than 12 hours has passed since the event. Better results are obtained if less than 6 hours have passed. Surgical complications increase with gangrene or delayed diagnosis; the latter favors treatment with heparin alone. Most patients with embolism are anticoagulated with warfarin before their heparin is stopped and stay on this lifelong.

Patients with thrombosis are usually not treated surgically because of the physical length and adherence of the thrombus. Because of pre-existing chronic occlusive disease, these patients usually have superior collateral circulation and therefore tolerate the acute occlusion better. Patients are treated with heparin as above. Lysis of the thrombus with thrombolytics (Streptokinase, t-PA) may be attempted if no evidence of tissue ischemia exists. Complications are frequent even in well-selected patients. Patients are maintained on heparin drips after any thrombolytics to prevent rethrombosis.

CHRONIC ARTERIAL OCCLUSIVE DISEASE

The prevalence of intermittent claudication based on symptoms reported on standardized questionnaires in middle-aged and older patients has been variably estimated at 1% to 5.5%. If one includes asymptomatic patients with physical evidence of atherosclerosis (i.e., decrease in the ankle to arm systolic blood pressure ratio or diminished pedal pulses), the prevalence increases to 14% to 20% (5), increasing with age (6). A slight increase in prevalence occurs in males relative to females, diminishing with advancing age. Diabetes mellitus, cigarette smoking, hypertension, and hypercholesterolemia, as well as hypertriglyceridemia, have all been associated with the development of atherosclerosis (7).

Pathophysiology

Atherosclerosis is believed to begin with endothelial damage followed by an increase in serum lipid uptake by adjacent macro-

phages, as well as fibrin and calcium deposition. Aortoiliac disease typically begins at or just distal to the bifurcation of the aorta. Involvement of the distal aorta in combination with both iliac arteries is referred to as the Leriche syndrome. Patients experience bilateral claudication and impotence and may show atrophic changes in both legs. Aortic occlusive disease sometimes extends up into the region of the renal arteries. Though arteriosclerosis is a systemic problem, significant occlusions tend to be segmental. The other typical sites for segmental occlusions are the distal superficial femoral artery and the popliteal artery. Diabetic patients are at increased risk for more severe as well as more diffuse and rapidly progressive disease. Hypertension has been associated with arteriosclerosis, wherein the elevated intravascular pressure may lead to endothelial damage and the release of growth factors that stimulate proliferation in vessel wall smooth muscle (7). Patients with a total cholesterol of greater than 260 mg/dL have about twice the incidence of symptomatic claudication as those with levels less than 200 mg/dL (7). Smoking has been shown to be the single largest risk factor for the development of symptomatic claudication (7) due to vasoconstrictive effects, endothelial permeability, and effects on prostaglandin metabolism.

Clinical Presentation

History

Many elderly patients have evidence of occlusive peripheral artery disease without symptoms. Patients may advance from an asymptomatic state to exercise claudication, claudication at rest, and finally ischemic skin ulceration and gangrene. Fortunately, most patients who develop claudication remain stable without such progression. A patient will often find that to stop walking for a few minutes brings relief, allowing resumption of walking until the pain recurs.

Physical Examination

Femoral, radial, dorsalis pedis, posterior tibial, and brachial pulses may be diminished or absent. About 10% of the population lack palpable dorsalis pedis pulses, so knowledge of previous vascular exams can be helpful (8). An abnormal posterior tibial pulse has superior predictive value for detecting peripheral arterial disease. BP distal to a diminished pulse is helpful to gauge the degree of obstruction present. A hand-held doppler device along

With a measurement of the BP may locate impalpable pulses. Auscultation for possible aortic, renal artery and femoral artery bruits should be done. The ankle/brachial index (ABI) is a bedside method for screening and estimating severity of peripheral artery disease. A systolic blood pressure reading is obtained in the patient's posterior tibial artery and divided by the systolic reading in the brachial artery. A ratio greater than 1.0 is considered normal, with an ABI of less than 0.9 being 95% sensitive as an indicator of peripheral vascular disease. A ratio of less than 0.4 indicates severe disease. This index can be calculated at rest and after exercise and even combined with ultrasound flow measurements for greater sensitivity (9). The involved extremity may show some atrophy in the subcutaneous tissue along with a loss of hair and shiny atrophic overlying skin. Nails in the involved extremity may be thickened and brittle. More severe occlusions may demonstrate evidence of skin ischemia and ultimately gangrene.

Diagnostic Studies

Arteriography continues to be employed for investigation of any suspected occlusion. However, MRI angiography will play a greater role and is already the study of choice for those patients with contrast dye allergy. One of these tests is a prerequisite to any anticipated peripheral artery bypass or endovascular procedure. Ultrasound examination of the arterial system of the legs is a noninvasive initial screening test that can serve as a basis for beginning medical therapy such as pentoxifylline (Trental), versus a more aggressive approach.

Patient Management

Prevention

Cigarette smoking is the single strongest risk factor for atherosclerosis and symptomatic claudication. Ninety percent to one hundred percent of patients presenting for intervention for their claudication are current smokers. A mandate for the patient to stop smoking is appropriate, among the few such occasions in medicine today. In heavy smokers, the risk of ultimate amputation after revascularization attempts is 10 times that of non-smokers (10). It has been assumed that control of other known risk factors such as diabetes mellitus, hypertension, and obesity would decrease the chances of the development and progression

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of arterial atherosclerosis. However, controlled studies have not been done. Aggressive correcting of lipids and smoking cessation may actually cause a regression of lesions (11).

Therapy

Tertiary preventive measures are an important part of treatment of symptomatic cases. Exercise consisting of walking to the point of claudication several times each day has been shown to decrease symptoms and increase exercise tolerance. Pentoxifylline appears to increase red blood cell compliance and improve flow through partially occluded arteries. It was shown to increase the walking distance in a patient with chronic occlusive arterial disease, but its role is usually limited to milder disease and symptoms.

Symptoms at rest or evidence of impending limb ischemia warrant more aggressive therapies. Balloon angioplasty has been used to treat stenosis of the iliac, femoral, popliteal, and tibial vessels. Results are best in a large vessel with high flow rate at a relatively short occluded segment (e.g., less than 3 cm of the common iliac artery). It works by redistributing the plaque along the intima. Complication rates vary from 5% to 20% and consist of bleeding at the catheter insertion site, as well as thrombosis, embolization, vessel perforation, and dissection. Initial success rates with iliac arteries are 80% to 95% with a 5-year patency rate of 60% to 90%. Initial rates for femoral or popliteal arteries are 75% with about a 60% 5-year patency rate. A laser-assisted angioplasty is used if a guide wire cannot be threaded through the site of occlusion. Complications are similar to standard balloon angioplasty, except for an increased risk of vessel wall perforation and or dissection (3% to 12%).

Mechanical atherectomy devices are vessel catheters with distal cutting elements as the catheter is advanced. Recanalization occurs initially in about 80% to 90% of iliac as well as femoral or popliteal lesions and falls to 60% to 70% after 6 months. Complications are similar to balloon angioplasty, except that vessel perforation is more common. Intravascular stents are used in the treatment of vessel aneurysms and residual stenoses after one of the above procedures, most commonly in the iliac arteries.

Thrombolytic agents (Streptokinase, t-PA) are generally not effective in chronic arterial occlusive disease. However, they have been used successfully in acute thrombosis or embolism, even if underlying chronic occlusive disease is present.

Surgical revascularization efforts are reserved for patients who are either experiencing claudication at rest or who are suffering ischemic ulceration or gangrene. Patency rates are again superior for stenoses in the larger more proximal arteries. Stenosis of the aortoiliac area can be approached with an aortofemoral bypass using a Dacron prosthetic graft. This major surgical procedure requires infrarenal cross-clamping of the segment of the aorta and carries a significant operative mortality. However, the procedure has a long-term patency rate of 85% at 10 years. Alternative approaches are femorofemoral bypass or axilofemoral bypass (often combined with a femorofemoral bypass). The latter procedures carry much less perioperative morbidity and mortality, but result in lower long-term patency rates.

For obstruction at the superficial femoral artery, a femoropopliteal bypass procedure can be attempted, but results are poorer than for more proximal procedures. The patient's reversed saphenous vein is used to bypass the occluded segment. Prosthetic grafts carry a higher thrombotic occlusion rate. The procedure has a better long-term patency rate if the distal anastomosis can be made proximal to the knee. Patients with tibioperoneal occlusions can also be approached with a reversed saphenous vein bypass graft, but long-term patency rates are poorer even than for femoropopliteal procedures.

Amputation is still often necessary, particularly in the face of gangrene after endovascular and bypass procedures have failed. Rehabilitation potential improves with each limb joint spared. Ideally, the patient is allowed to naturally demarcate, which may take weeks and allows for the development of collateral circulation. Progression and level of necrotic skin changes are observed before choosing the level of amputation. Frequently, however, extending gangrene and sepsis force an earlier amputation.

THORACIC ANEURYSM

Underlying etiologies as well as management approaches differ depending on the site of the aneurysm (i.e., ascending, aortic arch, descending).

Pathophysiology

Ascending aortic aneurysms are most commonly secondary to cystic medial necrosis, which can be seen with the Marfan Syndrome

as well as with other disorders. Aortitis secondary to syphilis remains an important cause. Dilatation of the ascending aorta can produce aortic valve insufficiency secondary to enlargement of the valve root. Coronary artery outflow can also be compromised, producing myocardial ischemia.

Aortic arch aneurysms are usually secondary to atherosclerosis, although syphilis remains a significant cause. They are frequently extensions of descending aortic aneurysms.

Aneurysms of the descending aorta are usually caused by atherosclerosis, although some are caused by trauma and some mycotic aneurysms occur.

Prognosis varies by site of the aneurysm. Syphilitic aneurysms are more prone to rupture than those caused by atherosclerosis. Symptomatic aneurysm carries an increased risk of rupture. Size of the aneurysm also affects the risk of rupture as shown in Table 6.1.

Clinical Presentation

History

Thoracic aneurysms are more often symptomatic than abdominal aneurysms. Nevertheless, most patients with thoracic aneurysms are asymptomatic. Symptoms are more common if the aneurysm is expanding, often heralding rupture. Patients may experience interscapular upper back pain and may describe it as extremely severe and tearing in nature if dissection is occurring. Anterior chest pain may occur as well. A variety of other symptoms can also be produced due to compression of contiguous structures by the aneurysm as listed below:

<i>Symptom Produced</i>	<i>Structures Effected</i>
Cough and stridor	Compression of trachea
Hemoptysis	Rupture into bronchi or lung parenchyma
Dysphagia	Compression of esophagus
Hematemesis	Rupture into esophagus
Hoarseness	Compression of left recurrent laryngeal nerve
Face and arm edema	Compression of superior vena cava

Patients may present with symptoms of left-sided congestive heart failure because of aortic root dilatation or ischemic myocardial effects secondary to interference with coronary blood flow from the aneurysm.

Table 6.1.

Diameter of Ascending Aortic Aneurysm	Percentage of Rupture
<5 cm	2.3%
5–10 cm	11.5%
>10 cm	44.5%

Adapted from Forman JJ, Kurzweg FT, Broadaway RK. Aneurysms of the aorta: a review. *Ann Surg* 1967;165:557–563.

Physical Examination

A patient with a ruptured aneurysm presents with tachycardia, and evidence of poor distal tissue perfusion. An expanding pleural effusion is usually present with decreased breath sounds and percussive dullness. Intact thoracic aneurysms usually produce no specific changes on physical examination. The diastolic murmur of aortic regurgitation may be recognizable at the base of the left sternal border and distended neck veins if superior vena cava compression occurs. Rarely, compression may produce appreciable tracheal deviation.

Ancillary Studies

Chest x-ray is the initial study of choice for suspected aneurysm; anteroposterior and lateral views are required for assessment. Small aneurysms may not be visualized with conventional chest x-ray. A CT scan of the chest with contrast or MRI further delineates the anatomical location and the diameter of the aneurysm, both being necessary to decide on the aggressiveness of treatment. When surgical repair is planned, contrast aortograms are done, particularly to locate the origins of arterial branches.

Patient Management

Surgical repair of thoracic aortic aneurysms carries a significant mortality rate (5% to 10%) and morbidity rate, including a 3% rate of paraplegia secondary to spinal artery compromise with descending aortic aneurysm. For this reason, thoracic aneurysms less than 5 cm, if not enlarging, and especially in poor surgical candidates, are managed with observation and aggressive blood pressure control. Surgical repair is indicated if the aneurysm is (5 cm or more) or if it is symptomatic or enlarging. If the aneurysm is secondary to atherosclerosis, normalization of cholesterol values

may retard progression, although this has yet to be proved. Repair consists of replacement with tube grafts or, if involving the arch and not circumferential, Dacron patches. Ascending arch aneurysm repair entails cardiopulmonary bypass.

Early identification of thoracic aneurysms is important as the prognosis with surgical repair deteriorates considerably if the aneurysm has begun to dissect. Operative mortality is about 50%, and morbidity includes an approximately 8% incidence of paraplegia with attempts to resect acute dissecting aneurysms.

ABDOMINAL AORTIC ANEURYSM

The incidence of abdominal aortic aneurysm has been estimated at about 36 per 100,000 (12), more common in men and increasing with advancing age. About 20% of aneurysms, mostly those <4cm in diameter, do not expand over time. About 60% expand up to 0.5 cm each year; and about 20% of aneurysms expand to a greater rate. Aneurysms greater than 4 to 5 cm expand at a faster rate than smaller aneurysms. Increased diameter of the aneurysm, chronic obstructive pulmonary disease, and hypertension are all associated with rupture. Table 6.2 summarizes the correlation between size of the aneurysm and risk of rupture.

Pathophysiology

A 50% increase in the diameter of the vessel is needed to define an aneurysm. Ninety percent of abdominal aortic aneurysms are infrarenal. The true pathogenesis of these aneurysms is unknown. A multifactorial etiology, with genetic, hemodynamic, and biochemical factors affecting the vessel wall, is the most current accepted theoretical mechanism. An association exists between atherosclerosis and abdominal aortic aneurysms, but atherosclerosis of the vessel wall probably represents a secondary response to previous vessel injury.

Table 6.2.

Size of Abdominal Aortic Aneurysm	Percentage of Rupture in 5 Years
<4 cm	2%
4–5 cm	3–12%
>5 cm	25–41%

Adapted from Ouriel K, Green RM, Donayre C, et al. An evaluation of new methods of expressing aortic aneurysm size: relationship to rupture. *J Vasc Surg* 1992;15:12–20.

Clinical Presentation

History

Most abdominal aortic aneurysms are asymptomatic. Patients may experience a dull lower back or middle or lower abdominal pain, more likely if expansion is occurring. Some patients notice painless abdominal pulsations. Patients may present with symptoms of acute occlusion in the distal arterial circulation secondary to embolization. With rupture, the patient complains of excruciating, tearing back and flank pain, which can also be felt in the abdomen. Other symptoms may be secondary to ischemia of other organs such as syncope and paraplegia.

Physical Examination

Efforts to palpate and outline the abdominal aorta should be made on all patients over the age of 50 and especially in smokers and those with hypertension. Sometimes pulsations are visible on the external abdomen. Examination may be hindered by obesity or involuntary rigidity in the patient. The hallmark of abdominal aortic aneurysm on physical exam is the lateral expansion of the pulsatile mass. While checking for lateral expansion of the pulsatile mass, the examiner should attempt to estimate the diameter of the aorta with the two examining hands converging on the lateral aspects of the vessel. The normal-sized pulsatile aorta can be palpated in thinner individuals, but the examiner will be able to estimate its diameter at only 2 to 3 cm. Only about 40% of patients with abdominal aortic aneurysms have an associated abdominal bruit. Patients with abdominal aortic aneurysms are more likely to have evidence of popliteal and femoral aneurysms. Rupture usually occurs into the retroperitoneum. The patient will appear in varying degrees of shock depending on the size of the rupture, how much tamponade has occurred in the retroperitoneum, and the status of any other medical condition present. Deep ecchymosis in the flank will develop if rupture occurred into the retroperitoneum, but can occur into the peritoneum as well as into the abdominal viscera.

Ancillary Studies

Ultrasound examination is the study of choice for confirmation of a suspected aneurysm. Its sensitivity for aneurysm detection is 99%, and it provides a reasonable and reproducible estimate of

size (13). Ultrasound examination can be hindered by obesity or by gas in the bowel.

Cross-table lateral abdominal x-rays can be useful in an emergency setting for urgent confirmation of a suspected aneurysm, if calcification in the aortic vessel allows estimation of the diameter. It is not as accurate as are ultrasound and CT examination. CT scan of the abdominal aorta, while too expensive as a screening tool, is used for preparation for surgery. MRI is applicable if the patient cannot tolerate the intravenous contrast for the CT examination. It cannot be used if the patient has a pacemaker or intra-abdominal metallic clips.

Aortography is limited to cases in which the doctor is concerned about the status of some of the major branch vessels (renal, mesenteric) before operative intervention is started.

Prevention

Abdominal aortic aneurysms are also more commonly seen in males who smoke and who have hypertension. Detection and control of hypertension are crucial, and lower systolic and mean arterial pressure are goals in patients with known aneurysms. For abdominal aortic aneurysms greater than 4 to 5cm, detection and elective surgical repair of the aneurysm are associated with a dramatically reduced mortality compared with that of patients with ruptured aneurysms. Operative mortality from repair of nonruptured abdominal aortic aneurysms in multiple series has been 2% to 4%; 40% to 60% when rupture has occurred. The majority of patients with ruptured abdominal aneurysm die before reaching a hospital.

Management

Contraindications to elective surgical repair are recent myocardial infarction (less than 6 months), uncontrolled angina, severe chronic obstructive pulmonary disease, end-stage congestive heart failure, incapacitating irreversible neurological deficits, or a life expectancy of less than 2 years. Coronary artery disease is the largest contributor to perioperative and 5-year death rates after abdominal aortic aneurysm repair. Careful clinical questioning regarding symptoms that may represent angina or anginal variants is indicated, if not routine screening with cardiac stress tests. If coronary bypass procedures are anticipated, these are done before repair of the aneurysm is attempted.

General indications for elective surgical repair of abdominal aortic aneurysm are:

1. Aneurysm is symptomatic.
2. Aneurysm is greater than 5 cm in diameter. (Some recommend repair if aneurysm is greater than 4 cm, particularly in patients who are otherwise healthy.)
3. Aneurysm is expanding at a rate of greater than 0.5 cm each year.

If the patient is not presently felt to be a candidate for elective repair, follow-up clinical examinations along with repeat ultrasound examinations should be done every 6 months for aneurysms 4 to 6 cm and every 3 months for larger aneurysms. Such patients and their families need to be taught the symptoms of aneurysm rupture and expansion so that their potential urgent entry into emergency medical systems can be expedited.

Operative repair involves Dacron graft placement, sewn into place first proximally, then more distally. The aneurysm sac is left in place.

DEEP VENOUS THROMBOSIS (DVT)

Estimated incidence of DVT in the United States is 1 million to 5 million cases each year, and most of these are not detected and thus not treated. Patients with DVT may develop three potential complications.

1. Pulmonary embolism (PE) develops in 30% to 40% of patients with clinical DVT. Even though only about 30% of patients with untreated pulmonary embolism, and only about 10% of treated patients die from it, pulmonary embolism is believed to be this country's 3rd leading cause of death.
2. Postphlebitic syndrome, a lifelong swelling in the involved extremity, is seen in about 50% of patients who have had a DVT. This is usually minimal and can be appreciated only by checking a limb circumference and comparing this with the contra-lateral extremity. It can be more severe especially if the precipitating DVT was extensive, featuring significant dependent leg edema and sometimes even venous stasis changes in the skin or stasis ulceration.
3. Venous gangrene occurs only if a DVT is so extensive as to interfere with the arterial perfusion of the extremity by a back-log phenomenon. This is only rarely seen.

Pathophysiology

The increased likelihood of deep venous thrombosis development in patients with venous stasis, hypercoagulation states, or endothelial injury has been recognized since the 1800s. What has only recently been recognized, however, is that many patients are genetically susceptible owing to a point mutation in the gene for factor V, which causes them to have a poor anticoagulant response to activated protein C (14, 15). This hereditary thrombotic tendency frequently results in clinical thrombosis when the patient also has been exposed to one or more of the acquired risk factors mentioned below. Other genetic risk factors such as mutations in protein C, deficiencies in protein S, antithrombin III deficiencies, or homocystinuria have long been recognized, but play an etiologic role in only a small proportion of those patients with deep venous thrombosis. Genetic factors are more likely in patients with recurrent DVT or PE.

Acquired risk factor assessment is crucial in both the prevention and diagnosis of deep venous thrombosis because patients are often without symptoms and because physical diagnosis is notoriously unreliable. The following is a listing of acquired risk factors for deep vein thrombosis: previous deep venous thrombosis or pulmonary embolism; congestive heart failure or myocardial infarction; obesity; recent surgery; presence of malignant neoplasm; birth control pills; age greater than 65; endothelial vessel wall injury; venous varicosities.

The greatest postsurgical risk appears to be with hip and knee surgery followed by gynecologic/lower abdominal and spinal surgery. Malignant neoplasms are sometimes associated with a hypercoagulable state and sometimes even chronic disseminated intravascular coagulation. While higher dose estrogen combination pills carry an increased risk, it does not appear that standard estrogen replacement therapy after menopause carries such risk for DVT. (16).

Pregnancy, stroke, and trauma are risk factors. Risk with trauma is greatest with fractures, especially involving the hip.

Clinical Presentation

History

As many as 50% of patients have no symptoms. Symptomatic patients typically complain of a unilateral swelling of an extremity,

rarely bilateral, or of pain in the calf or thigh that might be worse with ambulation.

Physical Examination

Patients will sometimes demonstrate a low-grade fever. The overlying skin of the involved extremity may show increased warmth, distended veins that persist after elevation at a 45-degree angle, and visible edema. The calf may have a measurably increased circumference relative to the opposite side, and the skin of the involved extremity may be shiny and glistening. Tenderness may be elicitable in the involved deep vein sites, in the groove between the tibia and fibula, the popliteal fossa, the soleus muscle, behind the Achille's tendon and the inguinal area, and in the medial adductors in the thigh. Homan's sign carries poor specificity and probability value.

Diagnostic Studies

As the physical examination and history are frequently misleading in cases of DVT, suspected cases must be substantiated, based on imaging techniques, especially if the patients are felt to be at increased risk.

Ultrasound

2-D ultrasound evaluation for the presence of thrombi uses two methods for thrombi detection: 1. Direct visualization of the thrombi within the vein and/or of decreased compressibility in involved veins; 2. Demonstration that veins involved by thrombi are not as compressible as they are normally. Doppler color flow can be added to this study to detect any areas of altered venous flow. This test is time-consuming and requires experience on the part of technician and radiologist. Doppler flow may miss distal vein (calf) thrombosis (17) and some thrombi proximal to the groin. Sensitivity of the ultrasound study is only about 63% for asymptomatic thrombi. Nevertheless, as this test is noninvasive, does not use contrast dye, and does not require the patient to stand, it is the usual diagnostic study of choice.

Contrast Venography

Patients clinically likely to have DVT despite a negative ultrasound study should be considered for a contrast venogram if no

contraindications to the administration of the dye exist. Sensitivity and specificity are greater than 90%. However, reactions to the dye and iatrogenically induced thrombosis are possible.

Magnetic Resonance Imaging

MRI of the involved extremity may have comparable sensitivity and specificity to a contrast venogram and has the advantage of giving more information about the surrounding anatomy. It is helpful in diagnosing other causes of symptoms such as ruptured Baker's cyst. This examination is contraindicated in the presence of certain metallic foreign bodies in the leg and is significantly more expensive than the other modalities.

D-dimer test

This is a blood (plasma) test that has a 90% sensitivity for the presence of DVT, but a specificity of only about 50% (18). Some authors have proposed its use as an initial screen on patients suspected of having DVT or who are asymptomatic but carry a high risk.

Treatment of Confirmed Deep Venous Thrombosis

Patients are usually placed on a short period of bed rest (4 days or less) out of the assumed belief that ambulation might increase the risk of embolization and that after 4 days the thrombus has become adherent to the venous wall. Bed rest is not recommended for calf deep venous thrombosis as this might lead to propagation into the more proximal veins.

Compression stockings using a 30 to 40 mm Hg pressure gradient may decrease extension of the thrombosis.

Heparin

Treatment with an intravenous bolus of 5000 units of heparin is followed by a continuous intravenous heparin drip at 1000 units an hour. The drip is adjusted according to an activated partial thromboplastin time (APTT) every 6 hrs until the result is in the 60- to 85-second range. Once this is accomplished, monitoring with daily APTTs is necessary. Anticoagulation with heparin to this degree has been shown to greatly reduce the incidence of thrombus propagation and recurrence as well as pulmonary embolism if

Table 6.3.
Contraindications to heparin therapy.

ABSOLUTE
Known major bleeding diatheses (e.g., active gastrointestinal hemorrhage)
Central nervous system or eye surgery within the last 6 weeks
Known hypersensitivity to heparin
Within 48 hours of major abdominal or chest surgery
RELATIVE
Minor bleeding diatheses
Thrombocytopenia (absolute contraindication if platlet count is less than 50,000)
History of intracerebral hemorrhage
Uncontrolled severe hypertension
History of recent (diagnosed <8 weeks earlier) gastric or duodenal ulcer
Recent major trauma

adequate anticoagulation is to be achieved within the first 48 hours. Patients are at greater risk of complications from their DVT at inadequate anticoagulation levels of heparin than they are from bleeding complications from supratherapeutic levels. Table 6.3 lists contraindications to heparin therapy. As it becomes available, s q low molecular weight heparin will probably replace treatment with a continuous intravenous Heparin drip for DVT, as studies have shown it to be at least as effective, with a decreased incidence of bleeding complications, as well as being easier and cheaper to administer, requiring no follow-up APTT monitoring (19). Its use would also allow outpatient management earlier in selected cases.

Warfarin

As soon as the patient is anticoagulated on heparin, a loading dose of 10 to 15 mg of warfarin (Coumadin) each day should be given for 3 days. Heparin should be continued until the patient is therapeutically anticoagulated on warfarin, typically within 3 to 5 days. Once the 3-day loading doses are completed, maintenance doses of 2 to 5 mg of warfarin each day are required with daily prothrombin time (PT) checks until the patient is in the therapeutic range with an INR ratio of 2:3. Frequent PT checks are needed (at least weekly initially) even after discharge from the hospital. Oral warfarin is continued for 3 to 6 months (6

months if DVT was associated with pulmonary embolism). Life-long maintenance on warfarin is considered for patients who have had 2 or more episodes of DVT, or who have had one episode plus a known genetic predisposition or have anticardiolipin antibodies or lupus anticoagulant. Patients need to be monitored closely, as bleeding complications with warfarin are more common than with heparin. Patients need to avoid large amounts of vitamin K-rich foods (beef liver, broccoli, cabbage, cauliflower, spinach, lettuce) while on warfarin, as this can decrease the anticoagulant effect.

Inferior vena cava filters can be used in patients with known DVT who are producing pulmonary emboli despite known adequate anticoagulation.

Thrombolytic agents (Streptokinase, t-PA) are not usually used for DVT except for cases of extensive, proximal deep vein thrombosis that produce severe venous outflow obstruction and put the patients at risk for venous gangrene. In this setting, thrombolytics must be started within the first 24 hours and must be followed by full anticoagulation on heparin and later warfarin. Another proposed use for thrombolytic agents has been for the initial treatment of patients with DVT to diminish the risk of post-phlebotic syndrome. One study, however, has suggested that use of thrombolytic agents does not decrease the stasis changes of the phlebotic syndrome more than conventional therapy (20).

Prevention of DVT

This is a particularly important issue for DVT because of its subtle and frequently asymptomatic presentation. Higher risk patients can usually be identified, and appropriate prophylactic strategies implemented. The presence of multiple risk factors compounds the risk for the patient and warrants more aggressive prophylaxis. The following lists prophylactic regimens for those at risk for DVT. Treatment is started on the day of surgery or on the day of diagnosis and continued until the patient is ambulatory or has been discharged from the hospital:

High Risk	Prophylactic Method
Orthopedic surgery (includes hip fractures) (arthroscopic procedures carry less risk)	Low molecular weight heparin or adjusted dose s q heparin q 8 hr or warfarin

General surgery of lower abdomen or gynecologic surgery	Low molecular weight heparin or adjusted dose s q heparin or low-dose heparin.
Stroke	Low-dose or adjusted-dose heparin
Ischemic	
Hemorrhagic	Pneumatic compression boots
Major trauma with fractures	Low-dose s q heparin

Moderate Risk

General surgery of the upper abdomen	Low-dose heparin
Myocardial infarction, congestive heart failure	Low-dose heparin
Urologic surgery	Low-dose heparin
Neurologic surgery	Pneumatic compression boots

Low Risk

Pregnancy (Risk increased in postpartum period)	Early ambulation and graduated compression stockings
Low-dose heparin is dosed at 5000 units s q every 8 to 12 hours.	

Low molecular weight heparin has been even more effective than adjusted-dose heparin or warfarin in the prevention of DVT in patients undergoing hip and knee surgery (21). It has a long half-life and is usually given on a twice-daily regimen.

Adjusted-dose heparin involves monitoring the APTT after the patient is started on 5000 units of heparin s q every 8 hours and increasing the dosage each day until the patient's APTT is in the high normal range. Hemorrhage is the most common side effect (5% to 6% incidence). Thrombocytopenia may develop 3 to 14 days after treatment is started. Osteoporosis may occur after months of continuous therapy. Rare patients have developed hypersensitivity reactions, or a paradoxical thrombosis or alopecia on heparin.

Warfarin is usually started on the day of surgery for prevention of DVT, at a dosage of 2 to 5 mg each day without loading. Daily monitoring of prothrombin times is crucial to maintain an International Normalized Ratio of 2.0:3.0. Hemorrhage is also

the most common side effect from warfarin, with a risk of major hemorrhage more than with heparin (about 11%). The risk of major bleeding is increased if the patient is over 65, or has a history of stroke or gastrointestinal bleeding. Rare patients have developed skin necrosis or the purple toe syndrome on warfarin. Warfarin is contraindicated during pregnancy.

Multiple prophylactic measures can often be used concurrently and such use may be particularly appropriate for high-risk patients. The theoretical benefit is to diminish the venous stasis component that may predispose the patient to a DVT, even though he/she is on anticoagulants. Patients with significant arterial occlusive disease should not be on intermittent pneumatic compression, but most high-risk patients can be on a combination prophylactic approach (e.g., low-dose warfarin plus pneumatic compression boots).

The combination of pneumatic compression devices and graduated compression stockings has been shown to be synergistically effective in preventing DVT, and would be the prophylactic method of choice for those with contraindications to anticoagulants (22).

SUPERFICIAL THROMBOPHLEBITIS

This is a typically benign disorder that responds quickly to conservative therapy. In about 20% of cases, the thrombophlebitis can extend into the deep venous system, and rarely this has resulted in pulmonary embolism. The long saphenous vein is most typically involved. Superficial thrombophlebitis of the legs is sometimes seen if blunt trauma has occurred. Otherwise, it occurs in varicosities, in pregnancy, or the postpartum state, and rarely as an occult sign of malignancy. Superficial thrombophlebitis of the arm veins is most commonly seen with intravenous catheters and may develop during or after administration of irritating intravenous solutions (e.g., intravenous erythromycin). Septic thrombophlebitis is usually caused by *Staphylococcus aureus* or *Staphylococcus epidermidis* and is associated with indwelling venous catheters.

Clinical Presentation

History

The patient complains of pain or irritation in the region of the involved superficial vein. The patient may also complain of chills if he/she has septic thrombophlebitis.

Physical Examination

The superficial segment of vein is erythematous, and mildly indurated and tender. The overlying skin is warm to touch. In the case of superficial thrombophlebitis of the legs, the frequently varicose nature of the underlying vein can still be appreciated. The involved vein may become a palpable cord, and this may persist after treatment. Patients with septic thrombophlebitis will also demonstrate a high fever and may appear septic.

Diagnostic Studies

Because of the 20% prevalence of associated deep venous thrombosis, a 2-D venous ultrasound examination may be warranted. Thrombophlebitis of the saphenous vein is more prone to involve the deep veins, particularly if extension toward the saphenofemoral junction exists. If septic thrombophlebitis is suspected, 2 sets of blood cultures should be drawn.

Management of Superficial Thrombophlebitis

Patients should be encouraged to be ambulatory, as bed rest is feared (but not proved) to promote extension into the deep venous system. Irritating intravenous solutions should be stopped. Intravenous catheter sites should be removed if signs of local irritation exist. Resolution of symptoms in 1 to 3 days usually occurs with topical heat application and oral nonsteroidal anti-inflammatory medication. Surgical division and ligation of the vein (usually the saphenous) is rarely necessary. Anticoagulants are not indicated unless extension into the deep venous system is proved. Septic thrombophlebitis should be treated with appropriate doses of intravenous vancomycin pending culture results.

VENOUS VARICOSITIES AND SPIDER VEINS

The prevalence of venous varicosities is estimated at 20%, increasing with age and with pregnancy. Most patients do not have any attributable symptoms from these abnormal veins but do notice the cosmetic alteration they produce. Various veins are a risk factor for the development of superficial thrombophlebitis and or deep venous thrombosis.

Pathophysiology

Several predisposing features have been identified to explain development of superficial varicosities. A familial predisposition has been shown in 43% to 90% of patients with venous varicosities or venous telangiectasia. Defective venous valves are identifiable, but are not established as the primary cause. Varicose veins are primarily seen in the legs and in women who are or have been pregnant or in patients who have been doing heavy lifting or prolonged standing, and it is presumed this is related to exposure to elevated venous pressure in these groups.

Clinical Presentation

History

Most patients visually notice the dilated veins but do not notice any other symptoms. Less than 50% of patients complain of an aching, throbbing, or heavy feeling in the involved veins, and only 18% will report frequent symptoms. Patients complaining of calf or thigh pains must be evaluated for other potentially more serious etiologies, such as peripheral artery occlusive disease or deep venous thrombosis, before their pain is attributed to the venous varicosity. Pain due to varicosities is localized by the patient, and the pain/throbbing increases after prolonged standing and decreases with leg elevation. A particularly superficial portion of the varicosity may bleed externally with even minimal trauma, although this can be stopped with a topical dressing or Band-Aid and leg elevation.

Physical Examination

The tortuous, dilated superficial veins are usually readily visible, although palpation may be necessary if the patient has much subcutaneous fat. If the problem is of long-standing, chronic edematous changes may exist around the varicosities as well as the localized brownish skin discoloration of stasis dermatitis. Atrophy of the skin over the varicosities is common.

Diagnostic Studies

No diagnostic studies are necessary to arrive at the diagnosis. Doppler ultrasound is often employed prior to any surgical cor-

rection or sclerotherapy to identify the location of any incompetent valves.

Patient Management

Most patients are untroubled by their varicosities and spider veins and if not interested in sclerotherapy to correct the cosmetic alteration, can be reassured and monitored for disease progression or the development of complications. The use of elastic stockings may provide symptom relief for mild varicosities and may retard progression.

Sclerotherapy

This technique involves the intraluminal administration of a sclerosing agent to produce a chemical phlebitis, which, if successful, leads to eventual resorption of the treated vein (23). Care must be taken not to deposit the sclerosing agent outside the vessel wall, as this can produce scarring. A thrombus is produced in the vessel wall during this procedure, and the extremity is compressed and elevated after the injection to minimize its size and produce faster vein resorption. It is contraindicated in a patient with known predisposition to pulmonary embolism. Nevertheless, it is rare for this thrombus to embolize, and the patient's collateral circulation can usually compensate for the obliterated vessel without any significant disruption in venous return. Depending on the size of the vein to be treated, a small gauge needle (27–33) and 0.1 to a few ccs of sclerosing agent are used. The most common side effect from this procedure is cutaneous hyperpigmentation along the course of the resorbed vein, secondary to hemosiderin deposition, in about 30% of treated patients. It resolves in the vast majority of patients over the following months. Capillary dilatation adjacent to the treated vein develops in about 10%, and they usually must be treated with further sclerotherapy. Hypersensitivity reactions to the sclerosing agents and its preservatives (including anaphylaxis) have been reported. Bed rest is contraindicated after the procedure because of the fear of thrombus extension.

Vein Stripping

Surgical division and ligation of the involved veins is now an infrequent procedure since sclerotherapy is at least as effective for

most veins and does not involve as much pain, cost or time in the hospital. It still has a role if significant incompetence exists at the saphenofemoral or saphenopopliteal valves.

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Cerebrovascular Disease and Brain Injury

Elise M. Coletta

STROKE

Stroke remains the third leading cause of death in the United States. Approximately 555,000 strokes occur yearly in the United States, resulting in 140,000 deaths (1). Of the survivors, 300,000 are left disabled. At present 2 million to 3 million stroke survivors live in the United States (1). In 1993, the medical cost of stroke care in this country was \$17 billion. Stroke incidence and mortality rates increase with age. Overall, stroke mortality rates are decreasing. Although this is probably because of more effective treatment of hypertension, no good data exist to support this premise. Stroke incidence may also be decreasing for similarly unclear reasons. Prognosis after stroke varies with the site, size, and type of stroke, and the number of complications that may develop during the patient's acute and rehabilitative care. In general, patients with smaller events or early neurologic improvement do well, while those with hemorrhagic lesions do more poorly.

Risk factors for stroke include prior transient ischemic attack, advancing age, male sex, African race, diastolic and isolated systolic hypertension, cigarette smoking, diabetes mellitus, heavy alcohol use, obesity, sedentary lifestyle, atrial fibrillation (AF), myocardial infarction (MI), heart failure, left ventricular hypertrophy, peripheral vascular disease, and hypercholesterolemia.

Types of Stroke

Cerebral ischemia is the cause of 80% of stroke events. Two-thirds of these are thrombotic (large vessel or small vessel [lacunar]) in origin, and the rest embolic, either from a large vessel or the heart. Twenty percent of strokes are hemorrhagic in type. Intracerebral hemorrhage (ICH) causes 70% of these (i.e., 14% of the total); the rest are subarachnoid hemorrhages (SAH) (6%).

Causes of Stroke

Atherosclerosis is the cause of most ischemic strokes. Other etiologies (e.g., vasculitis, arterial dissection, antiphospholipid antibodies) should be considered in children, adults under age 45 and people without atherosclerosis risk factors. Cardioembolic stroke is often secondary to AF.

Hypertension is the major cause of ICH. Other causes are aneurysm, arteriovenous malformation (AVM), tumor, bleeding disorder, and in elders, cerebral amyloid angiopathy. Underlying aneurysm is the cause of 70% to 80% of nontraumatic SAH.

Patient Evaluation

Initial patient assessment should exclude confounding conditions (e.g., brain tumor, encephalitis, seizure, metabolic abnormality) and confirm the stroke diagnosis. Also, causal or contributing conditions that may affect initial management, or the development of complications, should be sought. The patient's symptoms and physical examination findings will help to determine the location, cause, and type of stroke. Symptomatically, hemorrhagic and embolic stroke events often develop suddenly. Conversely, thrombotic infarctions may develop slowly, or in a stuttering fashion, and often occur during sleep. Associated symptoms of intense headache, vomiting, mental status change, and nuchal rigidity suggest a hemorrhagic stroke, but are not universally present. The sudden onset of the worst headache ever, with or without loss of consciousness, followed by neck stiffness is highly suggestive of SAH. At least one-third of SAH patients will have a preceding minor (sentinel) aneurysmal bleeding episode. This can occur hours to days before a major hemorrhage, and is usually manifested by a sudden, unusual, but not necessarily severe, headache. Diagnosis and treatment of SAH at this early stage improves outcome.

Physical examination findings suggesting an anterior circulation stroke include aphasia, agnosia, hemisensory loss, and hemiparesis. Vertebrobasilar insufficiency is suggested by the development of ataxia, drop attacks, or severe dysarthria. Complete basilar artery occlusion may result in a locked-in syndrome, wherein the patient is conscious, but mute and quadraparetic.

Noncontrast computed tomography (CT), done at patient presentation, will usually detect SAH and will differentiate between ischemic and hemorrhagic infarctions in 95% of cases (2). If brainstem infarction or hemorrhage is suspected despite a negative CT, magnetic resonance imaging (MRI) may be helpful. Because stroke and MI can occur concurrently, serial cardiac enzymes are recommended. Cardiac monitoring is suggested for patients at risk for AF. A chest x-ray is helpful to evaluate cardiac status and detect an associated aspiration pneumonia. Appropriate routine laboratory studies include a complete blood count, electrolytes, glucose, blood urea nitrogen, creatinine, prothrombin and partial thromboplastin time, cholesterol and hepatic enzymes (2). If a nonatherosclerotic cause of stroke is considered, an erythrocyte sedimentation rate, syphilis serology, drug screen, and evaluation for a prothrombotic state should be obtained. If hypoxia is suspected, arterial blood gas analysis is required. Cerebrospinal fluid (CSF) analysis is indicated if SAH is suspected despite a negative CT. An elevated CSF pressure and grossly bloody or xanthochromic fluid are seen with SAH. ICH patients should not have a lumbar puncture because of the potential to precipitate brain herniation. Patients with neck pain, cervical spine tenderness, a history of head trauma or coma of unknown cause require a lateral cervical spine x-ray. If seizure is suspected, an electroencephalogram may be helpful. Duplex carotid imaging will detect the location and severity of carotid atherosclerosis, but may not accurately distinguish between vessel occlusion and very high-grade stenosis. Despite advances in MR angiography, many experts feel that arteriography is required for accurate evaluation of carotid disease prior to endarterectomy. Transthoracic echocardiography is useful if a high suspicion of cardioembolism exists.

Acute Management

Meticulous supportive treatment will maximize functional recovery after stroke. Cardiopulmonary stability should be achieved. To minimize the development of cerebral edema, fluid restriction

(1500 cc/day) is recommended for patients with large infarcts. Normal saline is the preferred intravenous fluid. Vital signs and neurologic status are monitored. Hypoxia, hypovolemia, hypotension, elevated temperature and hyperglycemia may all develop and should be treated promptly. Acute lowering of blood pressure is not recommended unless mean arterial pressure (sum of systolic blood pressure [SBP] + 2 [diastolic blood pressure] divided by 3) is >130 mm Hg, or SBP is >220 mm Hg (2). Less severe hypertension may require treatment if associated with acute MI, congestive heart failure, acute renal failure, dissection of the thoracic aorta, or ICH. Oral agents, such as captopril (Capoten) or nicardipine (Cardene), are preferred. Labetalol (Normodyne) and enalapril (Vasotec) are good parenteral choices. Sublingual nifedipine (Procardia) may precipitously lower blood pressure and worsen the neurologic deficit. The treatment goal in the first 24 hours is to reduce mean arterial pressure by 15% (2). Deep venous thrombosis prophylaxis is recommended for all patients with more than mild weakness.

Twenty-five to forty-five percent of stroke patients present initially with dysphagia, so an NPO status should be maintained until swallowing is evaluated. Elevating the head of the patients bed ≤ 20 degrees may prevent aspiration. Urinary dysfunction (retention and incontinence) and bowel dysfunction (constipation, impaction, and incontinence) can occur after a stroke and should be sought, evaluated, and treated (4). To prevent contracture, proper joint positioning and daily passive range of motion (ROM) joint exercises should begin promptly, followed by more active exercises. If the patient is neurologically stable, only 24 hours of bed rest is recommended (2).

Recent data suggests that intravenous treatment with tissue plasminogen activator, although associated with a significantly increased risk of symptomatic cerebral hemorrhage, will lessen the amount of acute damage after ischemic stroke if given within 3 hours of symptom onset (3). Heparin (to maintain the partial thromboplastin time between 1.5 and 2.5 times baseline) is useful in the treatment of acute cardioembolic stroke (2). A large infarction or uncontrolled hypertension contraindicate early anticoagulation. Acute use of aspirin, ticlopidine (Ticlid), or warfarin (Coumadin) has not proved useful, although extrapolated secondary prevention data point to a potential role for aspirin. One-quarter of all stroke patients deteriorate neurologically during

the first 48 hours. Unfortunately, no clinical or laboratory parameter can predict who will deteriorate, and no clearly effective pharmacologic agent is available to halt this process.

Unless the stroke is clearly hypertensive in etiology, the ICH patient should, at some point, have a contrast CT or MRI to rule out an underlying lesion. Surgical evacuation of a hematoma is an individualized decision. Only patients with large cerebellar infarcts or hemorrhages clearly benefit from early surgery.

SAH requires prompt referral to a neurological center. After SAH, blood pressure should be carefully lowered to prehemorrhage levels to avoid precipitating cerebral vasospasm. Prophylactic nimodipine (60 mg every 4 hours for 21 days) will halt the development of cerebral vasospasm, the greatest cause of morbidity following SAH. Seizure prophylaxis is commonly employed. Cerebral edema is treated with corticosteroids. Cerebral arteriography will definitively diagnose underlying aneurysm or AVM after SAH or ICH. The timing of aneurysm surgery depends on multiple factors. A major concern after aneurysm rupture leading to SAH is the development of rebleeding. The highest day-specific incidence of rebleeding is on day one (4%). Approximately 20% of surgically untreated aneurysms will rebleed within the first 2 weeks. Another complication of SAH, seen in approximately 15% to 20% of patients, is the development of symptomatic hydrocephalus. Three patterns of hydrocephalus can occur. Acutely obstructive hydrocephalus may require emergency ventriculostomy and external drainage. A subacute to chronic form of communicating hydrocephalus presents more insidiously, generally 4 to 20 days after SAH, owing to evolving permanent alteration in arachnoid CSF resorption. Chronic, often normal pressure hydrocephalus may be seen late in the patients course, and requires permanent insertion of an intraventricular shunt.

Functional Approach to Care

Early functional status assessment (activities of daily living [ADLs], mobility, instrumental ADLs, psychological and social resources) is important to identify all stroke-related disability. Addressing functional problems concurrently with the traditional aspects (e.g., pharmacologic therapy) of early stroke care will maximize patient outcome (4). Stroke-related disability has two causes: the neurologic impairment itself and the development of immobility-related medical complications (e.g., deep venous thrombosis,

pressure ulcers, deconditioning). Prompt patient mobilization and other preventive measures may prevent the latter (5). An elderly stroke patient may develop immobility-related medical problems after only 3 to 5 days of inactivity.

Stroke rehabilitation programs are available in different settings (e.g., hospital level unit, skilled nursing facility) and will benefit most stroke patients. The choice of setting is dictated by availability and an assessment of the patient's rehabilitation potential and social supports.

Chronic Care

Fifty percent of stroke patients surviving their initial event are alive 7 years later. Several chronic problems are common in stroke patients. Shoulder pain may be caused by frozen shoulder, shoulder subluxation, tenosynovitis, subacromial bursitis, rotator cuff injury, brachial plexus traction injury, and reflex sympathetic dystrophy (RSD). RSD is a poorly understood process that presents 2 to 4 months after stroke with burning or aching limb pain, vasomotor skin changes, hyperesthesia, and distal extremity edema. Eventually, the extremity becomes contracted and atrophic. RSD treatment includes ROM exercises and paravertebral sympathetic ganglion block. Proper shoulder positioning and prevention of arm edema may prevent RSD and other shoulder problems. Thirty percent to sixty percent of stroke patients experience a clinically significant depression. Not uncommonly, depression may develop after hospital discharge, perhaps several years after the neurologic event. Antidepressant medication and supportive care are effective treatments. The stroke patient's sexual functioning may be affected by many factors: the actual neurologic impairment, comorbid disease, medication effect, performance anxiety, relationship stress, and other psychologic issues. Proactive education about sexual function, along with specific suggestions tailored to the patient's situation are helpful. The patient's caregiver and family may show evidence of stress and depression. Psychological support, proactive education, and the provision of instrumental assistance (e.g., home health aide) will aid family adjustment.

Stroke Prevention

Treatment of hypertension and cessation of cigarette use reduce stroke risk. Strict diabetic control and other lifestyle modifica-

tions (moderating alcohol use, lowering blood lipids, increasing exercise) do not clearly reduce stroke risk, but have significant general health benefits. For patients at high stroke risk, aspirin is an effective primary preventive intervention. Warfarin (to maintain the International Normalized Ratio [INR] at 2:3) reduces stroke risk in patients with AF. A less effective alternative is aspirin (325 mg/day). Screening for carotid bruits is important for all men and women in the atherosclerotic age range. Asymptomatic, selected patients (i.e., excluding high surgical risk) with greater than 60% carotid diameter stenosis who undergo carotid endarterectomy have a 53% decrease in the relative risk of stroke after 5 years when treated in centers with remarkable perioperative morbidity and mortality rates ($<3\%$) (6). The overall low stroke risk of these patients (about 2%/year), and, the higher year one-stroke rate in surgical patients dictate caution in generalization of this data. A carotid bruit is associated with significant carotid stenosis in $\leq 50\%$ of cases.

For AF patients, warfarin (to maintain the INR at 2:3) will reduce the risk of recurrent cardioembolic stroke. Aspirin (325 mg/day) is less effective. Sound data do not support warfarin use for symptomatic or asymptomatic patients with large artery stenosis. After TIA or minor stroke, aspirin (75 to 1300 mg/day) effectively reduces the recurrence of nonfatal stroke, MI, and vascular death. Ticlopidine (250 mg twice a day) is reserved for patients who are intolerant to aspirin or for aspirin failures because of its high cost and the risk of neutropenia. For secondary prevention after TIA or minor stroke, select patients with carotid diameter stenosis of 70% to 99% benefit from carotid endarterectomy (plus 1300 mg of aspirin daily) when treated in centers with $<6\%$ perioperative stroke and death rates (7).

TRAUMATIC BRAIN INJURY

Causes of Epidural and Subdural Hematoma

Subdural hematoma is typically caused by bleeding from the cortical veins bridging the inner and outer brain membranes. An acute subdural (symptoms within 72 hours of onset) is almost always traumatic in origin, and is usually associated with a skull fracture. An acute subdural hematoma in a younger person is often the result of high-speed head injury, as in an automobile accident. A chronic subdural (symptoms 10 days or longer after on-

set) may be atraumatic, or secondary to what was thought to be insignificant head trauma. An atraumatic chronic subdural is more common in people older than 50, in alcoholics, and in individuals with epilepsy. The presence of low intracerebral pressure (often because of intracerebral shunts) or a bleeding disorder is a risk factor for traumatic chronic subdural hematoma. Elders are especially prone to chronic subdural hematomas because brain atrophy leaves the bridging cortical veins stretched and more susceptible to rupture.

An epidural hematoma usually results from arterial bleeding, and is almost always traumatic in origin. Most often, epidural hematoma develops after low-speed, blunt head injury, as may occur from a fall or trauma from an object. The most common cause of epidural hematoma is laceration of the middle meningeal artery and vein from a temporal or parietal skull fracture.

Patient Evaluation

Up to 50% of patients with acute subdural hematoma are initially unconscious after their head injury. Half of them remain comatose at hospital presentation. Chronic subdural hematoma patients more often present with mental status changes or headache that has been slowly increasing over days to months. In the absence of head trauma, the differential diagnosis of subdural hematoma includes stroke, drug or alcohol intoxication, and, with indolent presentations, brain tumor, dementia or depression. To differentiate from stroke, subdural is more likely when lateralizing neurologic signs fluctuate, or when headache, obtundation, or confusion are out of proportion to focal neurologic signs. Severe focal neurologic deficits are uncommon from a subdural. Focal neurologic signs can be falsely lateralizing because the hematoma causes a brain shift with compression of the contralateral cerebral peduncle. Hutchinsons pupillary sign, the dilation of the ipsilateral pupil secondary to the pressure of the herniated temporal lobe on the third cranial nerve, is a more reliable, but not infallible, localizing neurologic sign.

Epidural hematomas usually accumulate rapidly, thereby producing coma within minutes, or, at most, a day after head trauma. The classic presentation of initial, brief, loss of consciousness, followed by a lucid interval, then recurrent obtundation, is present in less than 50% of patients. Other symptoms and

signs may include confusion, progressive headache, vomiting, ipsilateral pupillary dilation, aphasia, spastic contralateral hemiparesis, and seizure. As the hematoma progresses, the Cushing effect (a bounding, slow pulse with an increase in systolic blood pressure) can be seen.

A CT scan will visualize approximately 90% of acute subdural hematomas and will uniformly document the location of epidural hemorrhage. After 1 week, many subdurals will appear isodense and may be undetectable by a noncontrast CT. An MRI is then the preferred diagnostic test. Because a skull fracture is detectable on CT, skull films are rarely needed.

Acute Management

Initial treatment of head trauma patients should be directed toward resuscitation and cardiopulmonary stabilization. The rapidity and completeness of the initial neurologic examination are dictated by the patient's neurologic status. The most important aspects of brief, initial neurologic screening are the patient's level of consciousness (best measured with the Glasgow Coma Scale [8], motor function and eye findings [pupillary size, shape, responsiveness and eye movements]). The Glasgow Coma Scale is the most sensitive tool for assessing overall brain function, and can also be used to estimate patient prognosis. Details of patient evaluation and management are beyond the scope of this chapter. Prompt neurosurgical evaluation is warranted.

Acute subdural hematoma, with mass effect apparent on CT, will typically require surgical evacuation, preferably by craniotomy in order to completely evacuate the clot. A small, chronic subdural hematoma, in the absence of neurologic symptoms and signs, may initially be watched closely via serial neurologic exams and CT scans. These lesions may resolve spontaneously. Overall mortality after subdural hematoma is approximately 50%. After acute subdural, adverse prognostic factors at the time of surgery include abnormal pupillary signs, decerebrate posturing, age greater than 40 years, and the presence of elevated intracranial pressure. Patients with an initial Glasgow Coma Scale score of 3 to 5 have a 75% mortality rate. Ninety percent of patients with an initial score of 12 to 15 make a good functional recovery. Seventy-one percent of patients with chronic subdural make a full functional recovery.

Epidural hematoma is a neurosurgical emergency. Death is inevitable unless surgery is performed. The placement of several burr holes, for drainage of the clot and ligation of any bleeding vessel, will often significantly improve the patient's neurologic status, even if initial neurologic deficits are severe. The presence of coma, bilateral positive Babinski signs, or decerebrate rigidity prior to surgery are poor prognostic signs for survival.

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Cardiovascular Problems in Children

J. Timothy Bricker and James C. Anderson

FUNCTIONAL MURMURS

Murmurs are extremely prevalent among children. Most normal children will have a murmur of some sort on routine examination. The conditions of examination (particularly how quiet and cooperative a child happens to be in a given situation) will result in a soft murmur being evident at some times and not at others. Functional murmurs are related to turbulence generated by rapid, although normal, blood flow. Increase in the intensity of most functional murmurs can be expected when cardiac output increases. Increase in cardiac output from fever, anemia, cutaneous vasodilation from exanthem, and anxiety are clinical features that often accompany primary-care visits and may serve to make a normal murmur louder. The murmur heard at the time of a febrile illness may sound softer and more characteristic of a normal murmur at subsequent examination when the child is afebrile. For this reason, it is often appropriate that the first referral for evaluation of a murmur in primary-care practice be to yourself (in order to have another listen following the acute illness and under better conditions for auscultation).

Confident identification of the common functional pediatric murmurs is the most important primary-care skill relating to the hearts of children. The majority of pediatric cardiac referrals are related to murmurs. Often the primary-care physician is correct in the assessment that the murmur is normal, but adequate certainty is lacking (either in the physician's mind or in the explanation to

the family) that the murmur is benign. Definitive recognition and expert communication with regard to a functional murmur and its significance by an astute primary-care doctor are high priorities for the provision of pediatric cardiac care of both value and quality.

Distinct characteristics of the functional murmurs in childhood can lead to confident identification of these murmurs.

Stills' Murmur

This murmur is the most common normal murmur in elementary school age children. It is named for George Frederick Stills, of the Great Ormond Street Hospital for Sick Children in London, who catalogued and classified normal murmurs in children in the early 1900s. A very loud Stills' murmur can suggest heart disease to even experienced observers. The Stills' murmur is systolic in timing. It is loudest at the left lower sternal border, but may also be heard at the apex or along the left sternal border. The pitch of the murmur is mid to low frequency. This murmur has been described as a "musical" or "vibratory" nature. The Stills' murmur sounds somewhat like a very short note from a cello string. The murmur is generated by vibration in the left ventricular outflow tract. Occasional cases of a Stills' murmur are associated with a false tendon traversing the left ventricle. Left ventricular false tendons are benign, and testing with a false tendon in mind is not warranted. The Stills' murmur is usually II or III/VI in intensity; increases in blood flow make the murmur louder. For this reason a Stills' murmur is characteristically louder supine than when the child is standing or seated. Respiratory variation is characteristic of a Stills' murmur, and the murmur is softer or gone with the Valsalva maneuver. The small child can be coached to hold her/his breath during gentle abdominal compression to simulate a Valsalva maneuver. Another technique is to clean the sphygmomanometer tubing and have the child blow the mercury column up to 30 or 40 mm. The Stills' murmur can be confused with left ventricular outflow obstruction. The murmur of hypertrophic obstructive cardiomyopathy is usually harsher with radiation to the aortic area and is louder standing than supine.

Pulmonary Flow Murmur

An early systolic crescendo-decrescendo murmur at the left second or third intercostal space is a typical murmur from increased flow across the pulmonary valve. The pulmonary flow murmur is

the typical high cardiac output state murmur in adolescents and young adults. This is one of the functional murmurs frequently heard in the third trimester of pregnancy. A functional pulmonary flow murmur should not radiate to the back or the neck. It is very important to ascertain that the murmur is associated with the normal inspiratory increase in splitting of the second heart sound. The pulmonary flow murmur is the same murmur that is heard with an atrial septal defect.

In the latter case, the splitting of the second sound is fixed.

Pulmonary Branch Stenosis Murmur

The pulmonary branch stenosis murmur is a soft, high-frequency, short systolic murmur, which is heard over the back, in the axillae, and laterally on the anterior precordium. This is a common murmur in the neonate and is particularly common in low-birth-weight infants. The lung gets very little flow in the fetal circulation, with the right ventricular output being pumped to the body through the ductus arteriosus, and thus, the pulmonary arteries are small. Postnatal remodeling of the pulmonary artery anatomy occurs gradually. The right-angle takeoff of the right and left pulmonary arteries is the source of turbulence that causes this murmur. Increased flow from a high cardiac output also will increase the intensity of this murmur. Physiologic anemia is the factor that commonly precipitates this murmur in infancy. The murmur may be suspected to be a small patent ductus arteriosus in a premature infant. The pulmonary branch stenosis murmur is usually gone by 6 to 8 months of age. An entity also occurs in which pathologic anatomic narrowing of the pulmonary artery branches is present. This type of pulmonary artery stenosis is seen with the congenital rubella syndrome, with Alligille syndrome (arteriohepatic dysplasia), and with other structural cardiac malformations.

Jugular Venous Hum

The murmur of a jugular venous hum is often heard first-hand when the child is examined while seated. The head size of a child is greater in proportion to the body than the head of an adult. The child's cerebral blood flow (and cerebral venous return) is also a greater proportion of the total cardiac output. The cerebral venous return through the jugular veins hits the innominate vein at a right angle. The turbulence generated is heard as a

low-frequency continuous murmur at the right and/or left infraclavicular areas. The “whirring” or “buzzing” noise of the jugular venous hum is obliterated with jugular compression or with examination of the child supine. The highest prevalence of the jugular venous hum murmur is among toddlers, but this functional murmur is often heard in older children. The continuous nature of this murmur can lead to its being confused with an arteriovenous fistula or a patent ductus arteriosus.

Carotid Bruit

The carotid bruit is another common physiologic murmur in children. It is caused by the same factors as a Stills’ murmur, and both murmurs are often heard together.

MURMURS ASSOCIATED WITH CARDIAC DEFECTS

Whereas confident and precise recognition of functional murmurs in childhood is essential for optimal primary-care practice, the precise anatomic diagnosis of the cardiac malformation associated with an abnormal murmur is not crucial. One should not be overly reassured by a lack of symptoms. Many congenital cardiac malformations are found in asymptomatic children. Normal growth and activity can be seen with even severe aortic or pulmonary stenosis or with a ventricular septal defect of moderate size.

Most newborns will have a transient murmur related to the ductus arteriosus, and newborns with serious congenital cardiac malformations are often not associated with a murmur. Tachypnea, cyanosis, or poor pulses are of much more concern from a cardiac standpoint in the nursery than is a murmur. The transient ductus murmur within the first day or two of life may be continuous or systolic only. Observation without further testing is generally adequate.

Atrial Septal Defect

The atrial septal defect (ASD) has the most subtle auscultatory features of any of the common congenital cardiac malformations and is the most difficult to recognize. The soft murmur of increased pulmonary blood flow is identical to the functional pulmonary flow murmur. Fixed splitting of the second heart sound is a characteristic auscultatory feature of an ASD. This loss of the normal inspiratory splitting requires optimal circumstances for

examination (including a quiet child) and experience in listening to the second heart sound. Recognition of an ASD by auscultatory features is not expected in infancy. Most ASD cases are identified at the preschool or kindergarten age. An atrial septal defect with a large left-to-right shunt will have a tricuspid area low-frequency diastolic flow rumble. Definitive diagnosis (sufficient for planning surgery) can be made by echocardiography, although both sensitivity and specificity may be poor in echocardiography laboratories with limited pediatric experience and expertise.

Ventricular Septal Defect

A ventricular septal defect (VSD) is the congenital cardiac defect most often diagnosed in primary-care practice. The murmur of a VSD is a harsh murmur that is loudest at the left lower sternal border. The murmur sounds rough because of the mixture of high- and low-frequency sounds in the murmur. Typically, the murmur lasts throughout systole and is about the same intensity throughout the cardiac cycle. A thrill is often felt along the left sternal border. The murmur of a ventricular septal defect is usually quite loud and is unlikely to be confused with a functional murmur.

An understanding of the natural history of patients with a ventricular septal defects is of practical benefit in primary-care practice. The newborn with even a large ventricular septal defect may not have a murmur in the nursery and will be unlikely to have symptoms of excessive pulmonary blood flow. The reason for this is that the fetal elevation in pulmonary vascular resistance drops gradually in the baby with a large ventricular septal defect. An appreciation of this concept is important because there is an understandable tendency to blame oneself (or one's practice partner) for having missed the diagnosis of a heart malformation that was present at the time of birth. Parents might also wonder why the obvious abnormality was missed on the newborn physical examination and are reassured by the appropriate explanation. As the pulmonary resistance falls, the pulmonary blood flow increases. A faint, low-frequency, rumbling murmur at the apex appears in diastole as the flow across the mitral valve during ventricular filling increases with the increase in pulmonary blood flow. "Heart failure" symptoms that develop in the baby with pulmonary overcirculation include tachypnea, pallor and sweating, fatigue with feeding, and poor growth. These symptoms develop from about 3 to 6 weeks of age. The term, congestive heart failure, itself can be un-

settling to parents, and an explanation of the cause and implications is in order.

Many babies with a VSD will have mild or no symptoms. This may either be due to a small size of the VSD or persisting elevation of the pulmonary vascular resistance. Spontaneous closure of a small VSD is common within the first year or two of life. Although spontaneous closure may occur later in life, it becomes progressively less likely with time. A VSD may generate more turbulence and become louder as it becomes smaller.

A child with a VSD can develop fixed elevation of pulmonary vascular resistance (Eisenmenger syndrome). This complication generally does not occur before 12 to 18 months of age in a child at sea level. In the days before the availability of heart surgery for children, primary-care doctors recognized a "golden period" in the life of a child with a large VSD in which a child with severe heart failure symptoms would become well balanced and seem more healthy by the early school years. Symptoms of advanced pulmonary vascular disease would follow, usually by the early teen years, which would include cyanosis, hemoptysis, syncope, arrhythmias, or sudden death. It is a mistake to confuse improvement in symptoms from increasing resistance and assume that the VSD is closing. Well before symptoms of pulmonary hypertension occurs, the physiology has become unsuitable for surgical correction.

The noncoronary cusp of the aortic valve rarely may be sucked into the VSD jet. Aortic insufficiency can complicate the natural history of even a small VSD.

The child whose examination suggests a VSD may have a more complicated cardiac malformation. The acyanotic form of tetralogy of Fallot, a well-balanced tricuspid atresia with a restrictive VSD, or VSD with subaortic stenosis are among the situations in which the recognition of features by physical examination may be quite difficult.

Endocarditis may complicate the natural history of a VSD. Endocarditis prophylaxis at the times of potential bacteremia is recommended according to the American Heart Association guidelines.

Pulmonary Stenosis

A harsh murmur at the left upper sternal border that radiates to the back is characteristic of pulmonary stenosis. An early systolic

ejection click (i.e., the murmur begins with a bang) is often associated in cases that have valvular stenosis. One may feel a thrill at the left upper sternal border and/or the sustained systolic lift of a hypertensive right ventricle along the left sternal border in more severe cases.

Pulmonary stenosis severity can confidently be followed by electrocardiography. The severity of right ventricular hypertrophy on electrocardiogram correlates well with the magnitude of the right ventricular to pulmonary artery gradient. Congenital pulmonary stenosis is not likely to progress in severity with growth. Treatment is by valvuloplasty in the catheterization laboratory in most cases that require treatment. Antibiotic prophylaxis is appropriate for this defect as well.

Aortic Stenosis

A harsh systolic murmur at the left mid-sternal border and at the right upper sternal border is characteristic of aortic stenosis. An early systolic click is often heard at the same locations. The aortic stenosis murmur characteristically radiates into the neck, and a suprasternal notch thrill is typical of aortic stenosis. This fact is of practical importance in primary-care practice. Absence of a suprasternal notch thrill provides reassurance that a suspicious murmur does not represent significant left ventricular outflow tract obstruction. The severity of aortic stenosis can be difficult to assess with confidence. Serial echocardiographic studies (and even catheterization) are more often needed with aortic valve disease than is the case for some of the other congenital cardiac defects. Congenital aortic stenosis may progress in severity in an unpredictable manner, but is particularly common during adolescent growth spurts.

Coarctation of the Aorta

The characteristic finding of coarctation on examination is diminished pulses in the lower extremities. An arm-to-leg blood pressure gradient can be detected with careful measurement of blood pressure in all four extremities. A delay in femoral pulsation is characteristic of severe coarctation in adults but will not be detectable in children with coarctation. Coarctation in the neonate is sometimes not detectable until the ductus closes. Delayed recognition of coarctation in primary-care practice is com-

mon. The murmurs associated with coarctation are not diagnostic. A continuous murmur over the back may be heard from collaterals. The common association of a bicuspid aortic valve often results in an ejection click or an aortic area systolic murmur.

Patent Ductus Arteriosus (PDA)

The continuous murmur in the pulmonary area that radiates to the back is easily recognized with a large ductus. A tiny ductus or a ductus in a child with an elevated pulmonary resistance is systolic only and difficult to recognize. Recognition of the ductus in the sick newborn requires a high level of suspicion and may require echocardiographic investigation. All PDA is hemodynamically significant in 20% of premature infants <1750 grams. The great majority of these can be closed medically by the use of indomethacin.

ENDOCARDITIS AND PROPHYLAXIS

Transient bacteremia is expected with dental procedures and with a number of surgical procedures. Antibiotic prophylaxis recommendations are outlined in Table 5.3. Findings of endocarditis are usually indolent and subtle. The increased risk of endocarditis is not a reason to delay antibiotic treatment for the child who has a cardiac defect and a focus for infection found on examination. Endocarditis should be considered in the differential diagnosis of a chronic or low-grade fever but should not alter plans for antibiotic therapy for the child with a probable source of bacterial infection.

RECOGNITION OF HEART DISEASE IN INFANCY

Congenital heart disease occurs in approximately 8 of 1000 live births. Rapid recognition and prompt intervention by the primary-care physician is crucial for an optimal outcome for a critically ill infant. Considerations of the infant's age and the symptoms at the time of presentation can help guide management.

Clues from Age at Presentation

The time at which newborns and infants with symptomatic cardiac defects present is related to postnatal circulatory changes. Babies presenting in the first 3 days of life have cardiac lesions rendering the infant unable to tolerate the transition from the fe-

tal to the postnatal circulation. Infants with transposition physiology will present with cyanosis. Others, such as critical aortic stenosis, hypoplastic left heart syndrome, interrupted aortic arch, and obstructed total anomalous venous return, may present with shock due to inadequate cardiac output.

Defects that present in the first 2 weeks of life include a number that become manifest from closure of the ductus arteriosus or postnatal decrease in the pulmonary vascular resistance. Ductal-dependent lesions include severe coarctation of the aorta, tetralogy of Fallot with severe pulmonary stenosis or pulmonary atresia, and transposition of the great arteries. Truncus arteriosus and large left-to-right shunts may become symptomatic in the first 2 weeks of life due to falling pulmonary vascular resistance and the onset of pulmonary edema. Most large left-to-right shunts will have a delay in decline of pulmonary vascular resistance and become symptomatic from several weeks to several months of age.

Clues from Presenting Signs and Symptoms

Cyanosis

Cyanotic heart defects often present at the time that the ductus arteriosus closes. Acrocyanosis is common in normal babies. Peripheral cyanosis can be seen in states of poor perfusion. Central cyanosis is noticeable around the range of 5 gms of desaturated hemoglobin. Polycythemia can cause the appearance of central cyanosis without significant arterial desaturation. Important degrees of desaturation can be unrecognized in the anemic baby. The neonate with cyanotic heart disease is often comfortable at rest and hyperpneic rather than tachypneic. Only a slight increase in arterial oxygen saturation usually occurs with administration of 100% oxygen. Cyanosis in the neonate from a pulmonary process may often have a clue about lung disease on the chest x-ray. Increased respiratory effort and tachypnea are common on exam. The step-up in arterial oxygen saturation with the administration of 100% oxygen is generally impressive, and an arterial PO_2 of over 100 torr is usual. With cyanosis caused by congenital heart disease, the infant is usually comfortable at rest, and 100% O_2 results in little if any increase in PO_2 . Stabilization and prompt referral to an appropriate cardiac center is imperative. Infusion of prostaglandin E1 at a dose of 0.05 to 0.1 micrograms per kg/min can be used to

keep the ductus arteriosus open for transport. Apnea is a common side effect of a prostaglandin infusion, and this possibility should be anticipated during transport. Delay in transport while attempting to obtain a precise anatomic diagnosis of the baby with a cyanotic heart defect is inappropriate. An echocardiogram in expert hands is usually definitive to guide plans for surgical treatment. Catheterization to open an atrial septal defect or urgent surgical intervention can be lifesaving.

Low Cardiac Output

Critical systemic outflow obstruction may present with hypotension, diminished pulses, poor perfusion, or acidosis. Cardiogenic shock at the time of ductal closure may occur in hypoplastic left heart syndrome and other situations in which the left-sided circulation is inadequate to sustain systemic perfusion.

Pulmonary Overcirculation

These babies will usually develop symptoms after the pulmonary vascular resistance drops. Ventricular septal defects and atrioventricular canal defects are the most frequent cause. Tachypnea, poor feeding, pallor and diaphoresis with feeding, and poor growth are characteristic. Prompt referral to establish a definitive anatomic diagnosis is important.

CHEST PAIN IN CHILDREN AND ADOLESCENTS

Chest pain is among the most common primary-care referrals to the cardiologist. The majority of cases can be confidently and safely managed by the child's primary-care physician. The pain is often described as sharp or stabbing. The pain can be a pleuritic pain that is worse with deep inspiration. Pain over the costochondral junction with chest wall tenderness to palpation is common. New physical activities (particularly weight lifting or with upper body conditioning) may be temporally related to the onset or the worsening of chest pain in young athletes. Exercise-induced bronchospasm is also frequently related to chest pain in young patients.

Extensive evaluation is not generally required. History and physical examination should provide adequate information for confident reassurance in the overwhelming majority of chest pain cases. One finds that the pain is generally frightening to the

child and concerning to the parents but is not overwhelming or unbearable in its severity. Reassurance alone is adequate therapy in the great majority of cases. One of the mistakes that may be made is to reassure the family that this benign chest pain will be transient. While this may be true in some cases, benign chest pain may last for years.

Further investigation is in order in chest pain reproducibly related to exertion. Exertional chest pain associated with syncope or lightheadedness is of particular concern. Pain with a typical anginal description in young individuals often is ultimately demonstrated to be benign, but appropriate investigations for congenital and acquired causes of coronary insufficiency are necessary. Some young children may complain of chest discomfort with episodes of supraventricular tachycardia. Description of heart racing or of heart pounding with chest pain will sometimes lead to identification of a paroxysmal dysrhythmia. Esophageal discomfort or even ulcer symptoms may be perceived as chest pain by young individuals.

THE CHILD WITH AN IRREGULAR HEART RHYTHM

An irregular rhythm is commonly noted in the primary care of children and is almost always benign. Respiratory sinus arrhythmia is frequent in childhood and is much more noticeable than in adults. This cause of irregular rhythm can be made by examination. Electrocardiography is diagnostic but generally not needed. Both atrial and ventricular premature beats are common in children as well.

Premature Atrial Contractions

Premature atrial contractions (PACs) are a cause of irregular rhythms in newborns. On electrocardiography, the PACs may be conducted normally (with the same QRS as the sinus beats), conducted aberrantly (with a wide QRS that can be confused with a premature ventricular contraction), or nonconducted. All three types of conduction may be seen on the same tracing. Whether a PAC is conducted normally, is conducted with aberration, or is blocked depends upon how early the premature atrial depolarizations occur. This electrocardiographic finding can be recognized with confidence in primary-care practice. These premature atrial contractions do not need additional investigation or treatment. Parents (and nursery personnel) can be reassured with

confidence. PACs in older children may also be found as a cause of irregular rhythm and are also benign.

Premature Ventricular Contractions

Premature ventricular contractions (PVCs) in older adult patients may be a marker for ischemic disease; in children, they are almost always benign. Features of benign PVCs in children include those that are single (i.e., do not occur as couplets or triplets), are uniform (the same morphology in the same lead), fixed-coupled (the same amount of prematurity), and disappear with exercise. PVCs seen in association with congenital or acquired heart abnormalities in childhood are of greater concern. Couplets, PVCs associated with symptoms, and PVCs associated with structural abnormalities require further investigation.

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Hypertension

David R. Rudy

EPIDEMIOLOGY AND PATHOPHYSIOLOGY OF HYPERTENSION

Prevalence figures for hypertension range as high as 20% of the U.S. population, but when defined as persistent levels of *diastolic* blood pressure (≥ 90 mm mercury (DBP), 3 of 3 determinations, the Hypertension Detection and Follow-up Program found a prevalence of 6.9 % among 158,906 patients screened (1). When systolic blood pressure criteria are included (SBP), (≥ 140 mm Hg, a prevalence intermediate between these two emerges (2). The concept of mean arterial blood pressure (MAP) encompasses both SBP and DBP and is calculated as $2/3$ the DBP + $1/3$ the SBP in mm mercury (Hg). MAP pressures in adults should be below 98. Hypertension is the ranking risk factor for strokes, alleviation of which reduces stroke, and other cardiovascular events as well (3). Hypertension is the cause of about one-third of cases of renal failure (Table 9.1).

Control Mechanisms

Blood pressure may be controlled directly by homeostatic mechanisms balanced mostly among intravascular diastolic volume, peripheral vascular resistance, aortic impedance, and cardiac output. The intimate involvement of kidneys in the physiology of hypertension is discussed separately.

Blood volume is normally protected on the low side in the kidneys by the actions of aldosterone as stimulated through volume and pressure sensors. The latter act through the renin-angiotensin system to form angiotensin III and in other ways to form other mineralocorticoids. Renin production is stimulated by beta adrenergic

Table 9.1.
Major causes of endstage renal failure.

Diabetic nephropathy	30%
Hypertension	25%
Chronic glomerulonephritis	20%
Polycystic renal disease	15%
Alport's syndrome	—
Obstructive uropathy	—
Interstitial nephritis	—

Reprinted with permission from Smith MC, Dunn MJ. Chronic Renal Failure. In: Rakel RE, ed. Conn's Current Therapy. Philadelphia: WB Saunders, 1995.

discharge in response to hypotension, volume depletion, salt restriction, and stresses, emotional and physical. Volemic elevation in blood pressure is blunted on the high side by suppression of renin, mediated through unclarified mechanisms, failure of which may lead to volume-dependent hypertension.

Peripheral resistance is maintained directly by alpha and indirectly by beta adrenergic stimulation, the latter to release angiotensin II through renin. In essential hypertension, renin production rises generally in concert with sympathetic stimulation and catecholamine production (4). Both alpha and beta stimulation may be thought of as responses to stress (5, 6, 7), or to renal ischemia. Sympathetic discharge normally is countered by parasympathetic stimulation and suppressed by carotid sinus stimulation. Cardiac output is regulated by alpha and beta sympathetic stimulation, and by diastolic blood volume.

Aortic impedance refers to stiffness. A certain degree of compliance allows absorption of the systolic pressure wave and protection of the peripheral circulation against excessive systolic pressures. Impedance is increased by atherosclerosis of the aorta, thus explaining much of the correlation of age with systolic hypertension.

Diagnostic Criteria and Staging

As agreed upon by the fifth convention of the Joint National Committee on hypertension (2), hypertension is defined as systolic blood pressure (SBP) ≥ 140 or diastolic blood pressure (DBP) ≥ 90 . These criteria require three readings on separate occasions, except

for ≥ 210 SBP/ ≥ 120 DBP, which defines hypertension stage 4 and requires immediate attention. Table 9.2 defines all stages. Malignant hypertension is defined as accelerated hypertension with papilledema. Normal blood pressures in children vary with advancing age. Table 9.3 shows the definitions of normal and elevated pressures at seven age ranges through adolescence.

ESSENTIAL HYPERTENSION

This is the name given to primary, as opposed to secondary, blood pressure elevation and comprises 90% to 95% of all cases. Hypertension is likely to become evident during the 5th or 6th decades, although clues usually have been apparent much earlier. Labile high-normal readings in youth carry nearly twice the relative risk for adult hypertension. The lack of persistence and the presence of positive family history for hypertension nearly always make early phase essential hypertension distinguishable from secondary hypertension (discussed later).

Essential hypertension can be subdivided into several varieties, based on the mix of pathophysiology involved. It varies along the continuum of sympathetic hyperreactivity versus salt/water retention. Even this is an oversimplified concept, as sympathetic alpha and beta activity in response to stress involve not only increased peripheral resistance and cardiac output but, through renin/angiotensin, salt, and water retention as well. Another factor is the presence of hyperinsulinemia, present in the insulin resistance

Table 9.2.
Staging of hypertension.

Category	SBP	DBP
Normal	<130	<85
High normal	130–39	85–89
Hypertension		
Stage 1	140–59	90–99
Stage 2	160–79	100–109
Stage 3	180–209	110–119
Stage 4	≥ 210	≥ 120

Modified with permission from The Fifth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V). Arch Intern Med 1993;153:161.

Table 9.3.**Normal and elevated blood pressures at seven age ranges.**

Age Group	High Normal (90–94th Percentile), mm Hg	Significant Hypertension (95–99th Percentile), mm Hg	Severe Hypertension (≥99th Percentile), mm Hg
Newborns (SBP)			
7 d		96–105	≥106
8–30 d		104–109	≥110
Infants (≤2 y)			
SBP	104–111	112–117	≥118
DBP	70–73	74–81	≥82
Children			
3–5 y			
SBP	108–115	116–123	≥124
DBP	70–75	76–83	≥84
6–9 y			
SBP	114–121	122–129	≥130
DBP	74–77	78–85	≥86
10–12 y			
SBP	122–125	126–133	≥134
DBP	78–81	82–89	≥90
13–15 y			
SBP	130–135	136–143	≥144
DBP	80–85	86–91	≥92
Adolescents (16–18 y)			
SBP	136–141	142–149	≥150
DBP	84–91	92–97	≥98

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syndrome, sometimes known as syndrome X (Chapter 31). Excessive insulin levels act to produce intravascular volume increases and, in certain cases, a heightened sensitivity to sympathetic discharge. The familial tendency of essential hypertension is especially evident for this group of patients. Against a given backdrop of the foregoing constitutional factors, BP is influenced by a number of dietary or environmental variables in addition to salt. They include calcium, insufficiency of which may raise BP, and lead levels of which even within the subtoxic range may be directly related to a tendency for hypertension (8).

General Therapeutic Goals in Essential Hypertension

Table 9.4 shows the JNC-V guidelines for follow-up at first encounter for the spectrum of blood pressure. Generally, when blood pressure control is achieved, follow-up visits initially are weekly if BP had been at stage 3 or 4, biweekly if at stage 1 or 2. In either case, frequency of visits is decreased gradually to 3 months as control is achieved. It should never be less than 3 months if the patient is on medication. If the patient can be taken off medication and the BP remains normal for more than 4 weeks, the indication for drug therapy may be re-evaluated. Table 9.5 gives therapeutic targets for uncomplicated hypertension and for African-American, diabetic and other special cases, to be discussed. The following are general guidelines for common drugs in various clinical situations and are not substitutes for thorough familiarization with the details of information on each agent before prescribing:

Table 9.4.

Recommendations for follow-up based on initial set of blood pressure measurements for adults.

Initial Screening Blood Pressure, mm Hg ^a		
Systolic	Diastolic	Follow-up Recommended ^b
<130	<85	Recheck in 2 y
130–139	85–89	Recheck in 1 y ^c
140–159	90–99	Confirm within 2 mo
160–179	100–109	Evaluate or refer to source of care within 1 mo
180–209	110–119	Evaluate or refer to source of care within 1 wk
≥210	≥120	Evaluate or refer to source of care immediately

^aIf the systolic and diastolic categories are different, follow recommendation for the shorter-time follow-up (e.g., 160/85 mm Hg should be evaluated or referred to source of care within 1 month).

^bThe scheduling of follow-up should be modified by reliable information about past blood pressure measurements, other cardiovascular risk factors, or target-organ disease.

^cConsider providing advice about lifestyle modifications.

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Table 9.5.**Blood pressure objectives in various pathophysiologic states.**

Essential Hypertension: $\leq 130/80$ (JNC-V)

Hypertension in African-Americans: MAP ≤ 98 (MDRD, Klahr, 1994)

Diabetic Glomerulosclerosis: SBP $\leq 126 \pm 8$ mm Hg (NIH captopril study found that 140 mm SBP was associated with a much worse outcome)

Isolated Systolic Hypertension: SBP $< 143 \pm 17$ mm Hg (SHEP trial)

Nondiabetic Glomerulopathy: SBP $\leq 122 \pm 7$ mm Hg (MDRD study, Klahr, 1994)

Modified from Lee A. Hebert. In: Goals for blood pressure controls according to clinical state. A presentation over Ohio Medical Education Network: Recent advances in the diagnosis and management of hypertension. The Ohio State University. Presented October 27–28, 1995.

Diuretics. *Thiazide* diuretics may be step 1 agents in 35% of all cases and in African-Americans and the elderly, expecting a greater than 50% chance of success. While often effective in diabetes type II, they may precipitate or aggravate hyperglycemia, and in moderate dosages, cause potassium wasting over time.

Examples are hydrochlorothiazide (Hydrodiuril), hydroflumethiazide, benzthiazide and many others. They may be compounded with a potassium-saving diuretic such as triamterene (Dyazide, Maxide) or spironolactone (Aldactizide) in situations requiring hydrochlorothiazide in daily dosages >12.5 mg/day, especially in the elderly.

Indapamide (Lozol) is also an effective antihypertensive diuretic and exhibits a lesser degree of both the above side effects.

Loop diuretics such as furosemide (Lasix), butanide and ethacrynic acid are usually not effective in hypertension except when it is associated with renal failure.

Beta-Blocking Agents. *Beta-blocking* agents are valuable in individuals who exhibit apparent elevated catecholamines, as in labile states. They are more likely to occur in a person in his/her late 30s or 40s. They are especially applicable in situations of coexisting angina, because of their reduction in pulse and of myocardial demand and where history of supraventricular dysrhythmia exists. Beta-blocking agents may work well to control blood pressure in concert with diuretics, in the broad center of hypertensives with mixed physiology. Nonselective beta-blocking agents are contraindicated in decompensating congestive heart failure because

of their negative inotropic and chronotropic effects, and are relatively so in type I diabetes due to the blockading effect on gluconeogenesis and sympathetic responses to hypoglycemia. They are contraindicated in anyone with asthma, symptomatic or controlled by active drug therapy, and in symptomatic or demonstrable peripheral arterial disease. The undesirable effects in asthma, diabetes, and peripheral vascular disease may be attenuated greatly by using beta 1 selective blocking agents at usual dosages.

The commonly used nonselective beta-blockers include propranolol (Inderal) and nadolol (Corgard). The most common beta 1 selective blocking agents are the twice-daily dosing metoprolol (Lopressor) and the once-daily dosing atenolol (Tenormin). Many beta-blocking preparations have been developed. The most important considerations in choosing them, in the dosages recommended by the drug literature, are to know of their classifications as to selectivity and to be aware of relative and absolute contraindications. Labetolol has both alpha- and beta-blocking effects and is especially effective in African-Americans with hypertension.

Angiotensin Converting Enzyme (ACE) Inhibitors. Primarily, they are useful in the labile hypertensive with sympathetic hypertonicity, wherein hypertension is dependent on an activated renin-angiotensin system, as in up to 65% of Caucasian hypertensives to varying degrees. ACE inhibitors are rational first step choices in the majority of hypertensive patients. In addition, they are specifically indicated in coexisting heart failure owing to their afterload reducing effects and may be adjunctive in coronary insufficiency. ACE inhibitors have a special application in marginal renal insufficiency caused by hypertension and diabetes, signaled by microproteinuria. However, precautions are to be observed in more advanced renal failure, especially in the presence of congestive heart failure or hyperkalemia. While ACE inhibitors may be effective in blood pressure control when combined with diuretics, they should not be started simultaneously with them, and diuretic dosages should be reduced when ACE inhibitors are initiated. The side effects, in addition to pharmacologic effects, include angioedema and cough. The most commonly used preparations are capoten (Captopril), quinapril (Accupril), enalapril (Vasotec), and lisinopril (Zestril).

A new category of drug is the angiotensin II type 1 receptor antagonists (AT II₁ antagonists). Clinically, they have virtually the

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same actions as the ACE inhibitors and share their indications completely. Their advantage at this stage of development appears to be their availability as alternatives in individuals who cannot tolerate ACE inhibitors due to angioedema or cough (9).

Calcium Channel Blocking Agents (CCBs). These agents function equally well in low renin hypertension and in the vast middle zone of pathophysiology. Calcium channel blocking agents have coronary dilating effects and are therefore useful in treatment of hypertension that coexists with coronary insufficiency. Though they exhibit afterload reducing properties, they must be used with caution in the presence or likelihood of heart failure, due to their negative inotropy. The CCBs most commonly used in hypertension are diltiazem (Cardizem) and verapamil (Calan), both of which are available in sustained-release forms for less frequent dosing. Nifedipine (Procardia), the first member of the dihydropyridine class, has been prescribed in great volume as well. However, recent reports indicate that use of short acting nifedipine is associated with a threefold mortality in patients with known coronary disease (10). A rather complete listing of antihypertensive medications is found in the JNC-V publications (2).

The Minimal Diagnostic Evaluation Before Commencing Pharmacotherapy

This includes consideration by history and physical examination of the possibilities of secondary hypertension, including thyrotoxicosis, primary aldosteronism, renovascular hypertension, pheochromocytoma, polycystic kidney disease, and coarctation of the aorta (see section on secondary hypertension).

The record should show that the patient has been evaluated for all other cardiovascular risk factors, including smoking history, and for diseases that coexist with hypertension, especially diabetes, coronary artery disease, and cerebrovascular disease; and for family history of those conditions. Further, documentation must be made regarding complications of hypertension, especially congestive heart failure and renal failure.

The minimal physical examination includes fundoscopy for status of the optic discs and for retinal hemorrhages and exudates; auscultation of the heart for gallops; the lung fields for rales; the abdomen for renovascular bruit; checking for palpability of all peripheral pulses.

The minimal laboratory studies' prerequisite to starting drug therapy include complete blood count, serum creatinine and urea nitrogen, serum potassium, and urinalysis for evidence of infection, glycosuria and proteinuria. The reasons for these measures concern mainly the evaluation of renal function, status of target organ damage if any, ruling out of secondary hypertension and the detection of complications. Potassium determination is made to rule out primary aldosteronism *before* starting any antihypertensive medication because of their broad and lasting effects on renin. Other studies may be delayed to the second or third visits while blood pressure is being brought under control.

Accelerated and Malignant Hypertension

The definition of accelerated hypertension is a recent increase of BP to stage 3 or 4 ($\geq 180/110$) associated with *onset* of target organ damage. The latter are hypertensive retinopathy (hemorrhages or exudates), renal failure, or heart failure. Papilledema onset associated with change(s) of accelerated hypertension constitutes malignant hypertension. Untreated, the 2-year survival is less than 50%. Patients may present with headaches and occasionally seizures. The onset of accelerated hypertension in a known patient who was either normotensive or controlled hypertensive is cause to seek a source of secondary hypertension. Table 9.6 lists the medications employed in accelerated and malignant hypertension, parenteral and oral, as appropriate.

Hyperreactive Essential Hypertension

This category accounts for approximately 10% of cases of essential hypertension in Caucasians as determined in research studies (11). Renin is known to rise to great levels in renovascular hypertension. At much lower levels, in essential hypertension, the hormone shows a tendency to be distributed both higher and lower than in normotensives, for a given sodium load, with only about 55% falling into the normal renin category. The renin level under normal physiological conditions is inversely related to sodium intake, so that precise diagnosis is not practical in the clinical situation (7, 11). Hot reactors share characteristics of sympathetic hyperreactivity and elevated catecholamines and tend to have distinguishing personality characteristics, which include poorly expressed anger (12, 13, 14), the basis for earlier

Table 9.6.
Management of hypertensive crisis: emergencies and urgencies.^a

Drug	Dose	Onset	Cautions
Parenteral vasodilators Sodium nitroprusside	0.25–10 µg/kg per min as i.v. infusion; maximum dose for 10 min only	Instantaneous	Nausea, vomiting, muscle twitching; with prolonged use may cause thiocyanate intoxication, methemoglobinemia acidosis, cyanide poisoning; bags, bottles, and delivery sets must be light resistant
Nitroglycerine	5–100 µg as i.v. infusion	2–5 min	Headache, tachycardia, vomiting, flushing, methemoglobinemia; requires special delivery system because drug binds to PVC tubing
Diazoxide	50–150 mg as i.v. bolus, repeated, or	1–2 min	Hypotension, tachycardia, aggravation of angina pectoris, nausea and vomiting, hyperglycemia with repeated injections
Hydralazine	10–20 mg as i.v. bolus 10–40 mg IM	10 min 20–30 min	Tachycardia, headache, vomiting, aggravation of angina pectoris
Enalaprilat	0.625–1.25 mg every 6 h i.v.	15–60 min	Renal failure in patients with bilateral renal artery stenosis, hypotension

Parenteral adrenergic inhibitors

Phentolamine

5–15 mg as i.v. bolus	1–2 min	Tachycardia, orthostatic hypotension
1–4 mg/min as i.v. infusion	1–5 min	Paresis of bowel and bladder, orthostatic hypotension, blurred vision, dry mouth

Trimethaphan camsylate

Labetalol

20–80 mg as i.v. bolus every 10 min; 2 mg/min as i.v. infusion	5–10 min	Bronchoconstriction, heart block orthostatic hypotension
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Methyldopate

250–500 mg as i.v. infusion every 6 hr	30–60 min	Drowsiness
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Oral agents

Nifedipine
(not extended release)

10–20 mg PO, repeat after 30 min	15–30 min	Rapid, uncontrolled reduction in blood pressure may precipitate circulatory collapse in patients with aortic stenosis
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Captopril

25 mg PO, repeat as required	15–30 min	Hypotension, renal failure in bilateral renal artery stenosis
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Clonidine

0.1–0.2 mg PO, repeated every hour as required to a total dose of 0.6 mg	30–60 min	Hypotension, drowsiness, dry mouth
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Labetalol

200–400 mg PO, repeat every 2–3 h	30 min–2 h	Bronchoconstriction, heart block, orthostatic hypotension
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It is sometimes appropriate to administer a diuretic agent with any of these drugs. i.v., intravenous; IM, intramuscular; PO, orally; and PVC, polyvinyl chloride. Reprinted with permission from The Fifth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V). Arch Intern Med 1993;153:173.

findings of that trait in hypertensives compared with the remainder of the population (15). These patients are more likely to be younger, less likely to be obese and perhaps fitting the description of the Type A personality.

Therapy of Hyperreactive Hypertension

If blood pressure is *high normal* or stage 1 in a young person with labile or white coat readings, counseling for stress management may be adequate for lengthy periods. For counseling techniques applicable in primary-care practice see Chapter 49. Biofeedback and cognitive restructuring are most effective in the hot reacting patient and least effective in low renin, diuretic responsive hypertension.

Good choices for first-step drug therapy include angiotensin converting enzyme inhibitors (ACE inhibitors) or beta-blocking drugs. Theoretically, diuretics are least effective in pure forms of this type. Calcium channel blocking agents may or may not be helpful in individual cases.

Nontypeable Essential Hypertension

These are the bulk of hypertensive patients and exhibit mixed physiology. They comprise 50% to 55% of cases in Caucasians and one-third in African-Americans. To the extent that renin is incompletely suppressed, it is inappropriately normal; thus, it is apparently a driving force on the blood pressure. Many are hyperinsulinemic and tend to fall into the upper end of the weight spectrum. The latter, especially, exhibit a positive family history of hypertension and/or diabetes type II.

Therapy

Salt restriction is a management component of all hypertension, but particularly so in this category and low renin states. A no-salt-added diet results in approximately 4 gm (100 mmol)/24 hours, about half the average intake in the United States.

A combination of calcium channel blocking, beta-blocking or ACE inhibiting agents, often with a diuretic, characterizes the most effective regimen for this most common form of hypertension. Typically, these agents are added one at a time. Successful monotherapy may occur with a calcium channel blocker, usually started in nonsustained-release forms in divided dosages. After establishment of effective dosages, they are usually changed to ex-

extended-release forms (e.g., Cardizem SR 30, 60 or 90 mg and Calan SR 120 or 240 mg). ACE inhibitors may also succeed as single drug therapy or as second-step choices. If control is difficult to achieve with the foregoing, adding a diuretic usually makes the difference. The thiazide group is more effective than loop diuretics except in the presence of renal insufficiency with serum creatinine ≥ 2.5 mg/dL. Dosages greater than 12.5 mg daily should be supplemented with potassium but are seldom necessary. Hypokalemia is accompanied by increased risk of cardiac dysrhythmia and diminished effectiveness of the antihypertensive medication. If a thiazide diuretic precipitates hyperglycemia or gout, substitution of the diuretic indapamide (Lozol) may be effective.

Salt Sensitive (Low Renin) Essential Hypertension

One-third of the general population with essential hypertension, two-thirds of African Americans, probably two-thirds of elderly and many of those with impaired renal function fall into this category. The low renin state is presumed to be the result of homeostatic suppression of renin and occurs in response to the presence of non renin generated humeral substances that cause retention (and a degree of craving) of salt, hence water. Among causes of secondary hypertension, primary aldosteronism constitutes the quintessential low renin type. In primary hypertension unidentified mineralocorticoids and, to some extent, hyperinsulinemia, are responsible for salt retention (16).

Therapy of Salt Sensitive Hypertension

A constant in the management of this type of hypertension is dietary salt restriction and is most relevant in this category. If the diet has no apparent effect on the BP, salt intake can be ascertained by obtaining a 24-hour urine specimen for creatinine (to validate the collection) and sodium. Other indications for 24-hour urine collections in hypertensive patients are discussed in a later section.

A diuretic is the primary choice of drug. Hydrochlorothiazide (Hydrodiuril) has been effective in controlling this type of hypertension in dosages of 12.5 to 25 mg, uncommonly requiring 50 mg daily. At dosages of ≥ 25 mg daily potassium loss must be recouped, either by adding 20 to 40 (meq mmol) in any of several oral preparations or by a combination of antihypertensive and potassium-saving diuretics, such as triamterene (Diazide,

Maxzide), spironolactone (Aldactizide), or amiloride (Moduretic). Loop diuretics are much less effective against hypertension than thiazides, except when associated with serum creatinine >2.5 mg/dL (166 mmol/L).

Hypertension in African-Americans

Hypertension pathophysiology differs in African-Americans compared with Caucasians. Two-thirds, compared with about one-third of non-Hispanic whites, tend to have low renin states, amenable to diuretic treatment as a first step or an early choice.

The prevalence of hypertension in African-Americans is 1.3 times that of whites (17), and African-Americans have nearly twice the incidence of stroke. *Prevalence of stroke disease* is deceptively more balanced because it refers to those living with stroke (1.26 times that of Caucasians) (18), and reflects a greater mortality in blacks.

African-Americans' hypertension features greater degrees of peripheral vascular resistance, along with salt sensitivity, but it appears not to exhibit as great a degree of neurogenicity.

For given levels of blood pressure elevation, African-Americans are at greater risk for renal failure. Blacks are represented 2.5 to 6.3 times their proportion of the population in end stage renal disease (ESRD) (19, 20).

Therapeutic Approaches to Hypertension in African-Americans

The therapeutic goals for blood pressures in African-Americans are set lower than in whites, reflecting blacks' lower thresholds for renal function deterioration at given heights of blood pressure. Thus, maximum MAP of 92 (125/75 mm Hg) should be attained (Table 9.5). It has been shown that renal function falls off precipitously with MAPs >98 in blacks, while in whites the decrement continues downward at the same rate.

Because of blacks' labile renal function in the face of hypertension, they should have more frequent follow-up in the outpatient setting than other patients for a given set of clinical circumstances. Salt restriction is even more relevant in blacks than in whites. Other nonpharmacologic treatments may be attempted in high normal BPs, consisting of stress reduction and physical exercise.

Diuretics and CCB agents are more likely to produce results

in blacks than in whites, while ACE inhibitors, beta-blockers and angiotensin-receptor antagonists less likely, a possible exception being the alpha-beta blocker labetalol.

Systolic Hypertension and the Elderly

This tends to be based on increased impedance and is more likely to be a low renin state, both of which are associated with advancing age. DBP normally does not rise appreciably with age or may even decrease. The rapid onset of diastolic hypertension in a patient >65 years old may signal atherosclerotic renovascular disease or, less commonly, showers of emboli into the renal vasculature from an aortic aneurysm. Sixty percent to seventy percent of the U.S. population are hypertensive by JNC-V definitions (Table 9.2). To the extent that it is a high-volume state, systolic hypertension responds to diuretics and less well to beta-blocking and ACE inhibiting agents. Achievement of the goal of SBP $\leq 143 \pm 17$ (SD) resulted in a 33% reduction in stroke and 25% reduction in myocardial infarction compared with SBP of 155 mm Hg in the SHEP trial (Table 9.5.) (21).

Treatment of Systolic Hypertension

A low-dose diuretic in the form of hydrochlorthiazide is effective in the great majority of white hypertensive patients >65 years old. Potassium-sparing activity is crucial in the elderly even at low dosages. African-American patients in the same age group may require high dosages (25 to 50 mg) with appropriate coverage for potassium. If diabetes or renal failure coexist, preservation of renal function must enter into the overall plan.

Hypertension, Insulin Resistance (Syndrome X) and Type II Diabetes

Insulin resistance is said to be based on suppression of insulin receptors, aggravated or caused by obesity, a characteristic of diabetes and prediabetes type II. Hyperinsulinemia is thought to cause elevation of total and reduction of high density lipoprotein cholesterol; elevation of serum triglycerides, and elevation of BP. It appears that this hypertension tends in part to be of the salt sensitive, normal, or low renin type. Hypertension coexists frequently with type II diabetes in individuals and families. It may be

inferred that the hypertension in a type II diabetic will respond equally well as the diabetes itself to weight loss.

Calcium channel blockers may be effective as single drug therapy. Diuretics also may be effective as single agents but owing to the tendency of thiazides to aggravate or (precipitate) diabetes, they are usually held back as a second or third drug in diabetics. If blood sugar control is worsened by a thiazide, indapamide is a reasonable substitute, being less likely to show that effect. If renal insufficiency is evident, an ACE inhibitor is indicated even if the patient's blood pressure is otherwise controlled.

Hypertension in Women

Women are subject to the same prevalence of essential hypertension as men, but women tend to have lower renin activity in hypertension, and thus have a greater likelihood of salt sensitivity. Oral contraceptive use is associated with a mean increase in BP, more likely when a positive family history of hypertension exists. Female patients who smoke are best advised to stop oral contraceptive use at the age of 35, due to the compounding effect of atherosclerotic risks (Chapter 18). Treatment approaches are the same as with males. Hypertension in pregnancy is not addressed in this work.

RENAL PATHOPHYSIOLOGY, GLYCEMIC CONTROL, AND HYPERTENSION

The physiology of hypertension is intimately connected with that of the kidneys and with glucose metabolism. Hypertension is a leading cause, along with diabetes and chronic pyelonephritis, of chronic renal failure and of end stage renal disease (ESRD) (Table 9.1). Rate of progression of renal disease in hypertension is inversely related to blood pressure control as defined as MAP over time. Creatinine clearance in normal adults is 85 to 125 mL/minute, depending on lean body weight. Small women are at the low end and muscular men at the upper end of the range. Creatinine clearance is sometimes expressed as mL/min/1.73 m² (the surface area of the average person). In adult life creatinine clearance deteriorates normally at the rate of approximately 1 mL/min/year so that an expected rate of creatinine clearance at age 70 is approximately 70 mL/min.

Advancing renal disease in both hypertension and diabetes is first signaled by microproteinuria; 30 to 300 mg/24 hours in diabetes (22); 200 to 500 mg/24 hours in hypertension (23). As protein loss in hypertension reaches 1 gm/24 hours, creatinine clearance is likely to be in the range of 25 to 50 mL/min and be deteriorating at the rate of 2 to 4 mL/min/year. In patients with hypertensive renal disease, control of blood pressure to a target of 92 mm Hg MAP (125/75 mm Hg) was shown to retard the reduction of creatinine clearance by approximately 1 mL/min/year, a reduction of 25% to 50%. This would affect an estimated delay in ESRD at 5 years (24). Equally effective was reduction of dietary protein intake from an average of 1.3 gm/kg to approximately 0.6 gm/kg. That effect in hypertensive renal disease was demonstrated only when proteinuria had reached the rate of 1 gm/24 hours, confirmed by repeated collection. The recommendation for practice is reduction of protein intake to 0.75 gm/kg. In addition, glomerular filtration rate (GFR) is preserved by 3.7 mL/min/year for each 10 mm Hg reduction in MAP. An ACE inhibitor preserves GFR by 3.4 mL/min/year beyond that achieved by BP reduction by other means (25). Reduction in protein intake to roughly this same level has a similar ameliorating effect on the progress of renal disease in diabetes without hypertension.

In addition to their adverse effects on cardiovascular risk, hypertension and diabetes each acts to destroy renal function. Ten percent of type II and 30% of type I diabetics develop ESRD (26). Given the heavy association of type II diabetes with essential hypertension, a strong case can be made to consider baseline 24-hour urine studies in newly diagnosed type II diabetics and obese hypertensive patients as well as periodically (e.g., every few years) in established hypertensive and diabetic patients as discussed earlier and in Chapter 31. This would allow determination of kidney function (creatinine clearance), detection of significant proteinuria, and measurement of dietary intake of sodium and dietary protein all in the same specimen.

Creatinine clearance is calculated as follows:

$$C_{cr} = [U_{cr} \text{ (mg/dL)} \times 24 \text{ urine volume in mL}] / [\text{plasma Cr (mg/dL)} \times \text{time (min)}], \text{ where Cr = creatinine; } C_{cr} = \text{clearance of creatinine; } U_{cr} = \text{urine creatinine.}$$

Creatinine clearance is *estimated*, requiring only serum creatinine and anthropomorphic data as follows:

$$C_{cr} = [(140 - \text{years of age}) \times \text{weight in Kg}] / 72 \times \text{serum creatinine.}$$

The formula for calculation of protein intake, given dietary state is as follows:

$$\begin{aligned} \text{Dietary protein (grams)} &= [\text{UUN \{grams\}} / 24 \text{ hr} + \\ &\quad (0.031 \times \text{lean body weight \{Kg\}})] \times 6.25, \\ \text{where UUN} &= \text{urine urea nitrogen; } 0.031 = \text{grams fecal} \\ &\quad \text{nitrogen} + \text{urinary non-urea nitrogen/kg body weight/day;} \\ &\quad 6.25 = \text{grams of protein/gram of nitrogen in protein.} \end{aligned}$$

Management of Hypertension with Chronic Renal Failure

Patients with advancing renal failure tend to have hypertension of the low renin type in which salt restriction becomes a key part of management. Salt should be aggressively restricted, to 3 to 4 gm/24 hours (70 to 100 mmol).

Proteinuria itself is damaging to renal function. The salutary effects of dietary protein reduction as well as ACE inhibitors were outlined earlier.

Diuretic antihypertensive drug therapy is indicated at step one or step two. However, if creatinine has risen to 2.5 mg/dL (166 mmol/L), a loop diuretic may be required to achieve control, along with other aspects of management of renal failure.

SECONDARY HYPERTENSION

The overall category accounts for 5% to 10 % of all cases (27). In this, the text interests itself with recognition, diagnosis, intelligent referral, and awareness of the main aspects of definitive management by consultants. For greater depth and total management, the reader is referred to *Nephrology*, the House Officer series (28). The more severe and difficult to control, the more likely it is secondary hypertension.

Renal Parenchymal Hypertension

This category may account for 5% of all hypertensive patients or about half of secondary hypertension. Hypertension incompletely controlled may lead to loss of renal function through nephrosclerosis. Conversely, renal hypofunction of any cause can lead to hypertension. A significant percentage of these cases are secondary

to chronic infection, often present since childhood. Issues relevant to this subject were covered earlier. The principles of treatment are two: Early in the course, previously controlled hypertension may change to a higher renin state and require ACE inhibitors or beta-blocking agents. Salt restriction and diuretic therapy apply later in the course, characterized by rising serum creatinine and/or proteinuria $\geq 1\text{gm}/24\text{ hours}$.

Renovascular Hypertension

It accounts for 0.5% to 5% of all hypertension (27, 29) and is caused by renal arterial stenosis. It occurs in two main varieties, fibromuscular dysplasia, 80% of which occurs in women under age 20; and atherosclerotic renal artery stenosis, mainly in males over age 55. It is high renin hypertension in response to hypoperfusion as sensed by the juxtaglomerular apparatus of the afferent arteriole of the nephron. In bilateral disease, renal failure may occur with azotemia. In that case, the hypertension becomes volume dependent, and pulmonary edema may occur due to sodium/water retention.

Plasma renin activity ranges $\geq 5.7\text{ ng/mL/hour}$ in the captopril renin suppression test. Patients may present with accelerated or malignant hypertension and may exhibit an abdominal bruit over the involved renal artery. The kidneys may be asymmetrical with a length difference of 1.5 cm or more. Besides the captopril renin suppression test findings, the captopril renogram in renovascular hypertension shows a decrease in GFR without a corresponding drop in renal blood flow. The definitive test, signaled by the foregoing positive screening tests, is the renal arteriogram, which discloses $\geq 75\%$ stenosis.

Percutaneous transluminal angioplasty is successful in 80% of nonostial lesions, while ostial lesions show $<20\%$ success (27, 29). Surgical revascularization is available for unsuccessful cases. Nephrectomy may cure those with an atrophic nonfunctioning kidney.

Primary Aldosteronism

Hypertension is produced by autonomous secretion of aldosterone. This comprises 0.1% to 1.0 % of cases of hypertension. Of these, 70% to 90% are due to solitary adenomas (aldosterone-producing adenoma, APA). The remainder are virtually all due

to bilateral hyperplasia (idiopathic hyperaldosteronism, IHA) except for rare unilateral hyperplasia cases and more rarely, adrenal carcinoma. The hallmarks are hypertension with hypokalemia (\pm metabolic alkalosis), minimally diuretic induced severe hypokalemia, and suppressed PRA in the presence of elevated aldosterone levels. Effects secondary to hypokalemia include insulin resistance (\pm hyperglycemia) and orthostatic hypotension. Further laboratory screening includes a 24-hour urine potassium (>30 mmol) and saline aldosterone suppression test (failure to suppress angiotensin II and PRA after a saline intravenous load). The postural stimulation test shows an elevated baseline aldosterone level in both APA and IHA. Normals and IHA patients show an increase in serum aldosterone with orthostasis, while APA shows an elevated baseline level but failure to rise further with orthostasis.

Once screened, a CT scan of the adrenal area will delineate an adenoma but only if ≥ 1 cm diameter. If no mass is seen on the CT scan, an adrenal venous sampling test is done. After ACTH infusion, the side containing an APA shows a high blood aldosterone:cortisol ratio, while on the contralateral side the ratio is low. In IHA, the ratio is high on both sides.

APAs are treated by excision, which results in normalization of pressure in 50% to 75% of cases. IHA is treated best by the use of an aldosterone antagonistic agent, spironolactone or amiloride, with resultant correction of blood pressure and hypokalemia.

Pheochromocytoma

These are tumors of chromaffin cells that elaborate epinephrine or norepinephrine. They account for 0.1% to 0.4% of cases of hypertension. While 85% of normal adrenal medullary secretion is epinephrine, approximately 60% of the catecholamine secreted by pheochromocytomas is norepinephrine. Norepinephrine stimulates α_1 receptors to cause sustained hypertension. Epinephrine stimulates α_2 receptors to produce the classic paroxysmal attacks associated with the disease. Ten percent are located in an extra-adrenal site (90% intra-adrenal); 10% are bilateral, and 10% familial. Familial cases tend to occur in association with medullary carcinoma in multiple endocrine neoplasia (MEN) 2. In MEN 2A, pheochromocytoma occurs also with hyperparathyroidism and in MEN 2B with mucosal neurofibromatosis (30).

Historically, patients are likely to manifest sustained hyper-

ension (60%) or accelerated/malignant hypertension or myocardial infarction. A significant minority present with paroxysmal headache, tremulousness, tachycardia, and less commonly hypotension.

If symptoms are nonparoxysmal, diagnosis is made by a single 24-hour urine specimen for free catecholamines, metanephrines, and vanillylmandelic acid (VMA). If symptoms are paroxysmal, the urine collection must coincide with the day of an attack. By testing for three agents, sensitivity and specificity are acceptable. False positive results occur with certain medications, especially sympathomimetic and monoamine oxidase inhibiting agents.

Treatment consists of medical control of hypertension and fluid repletion. Beta blockade is avoided until control is achieved with alpha blockade, to avoid precipitation of attacks due to compensatory alpha discharge. Phenoxybenzamine (Dibenzyline) and prazosin (Minipres) are the usual agents. Labetalol is acceptable because of its combined alpha- and beta-blocking actions. After pressure control has been achieved, beta blockade is needed throughout the operative period for control of dysrhythmias. A nitroprusside drip during surgery guards against rebound hypotension at the moment of relief of the tumor.

Polycystic Kidney Disease

Renal cysts have five basic types: simple cysts, autosomal recessive polycystic disease, autosomal dominant polycystic kidney disease (ADPKD), medullary sponge kidney, and medullary cystic kidney disease. All but simple cysts are medically significant for such symptoms as hematuria, urinary tract infections, or urolithiasis.

ADPKD manifests hypertension in more than half of cases. It occurs in a lifetime incidence of 1:600, exhibits a family history in 75%, is characterized by abdominal pain and/or hematuria in a majority of cases, and leads inexorably to renal failure (31). Ten percent to thirty-five percent have cerebral aneurysms, and 10% to 20% have nephrolithiasis. The hematocrit may be higher than normal due to production of erythropoietin. Diagnosis is based on abdominal CT findings, if not by renal ultrasound. The latter is favored in screening for economy but is limited in sensitivity to cysts of ≥ 0.5 cm.

The hypertension is generally renin-angiotensin driven, with salt sensitivity becoming more important as renal insufficiency develops. Alpha- and beta-blocking agents or CCBs are effective

early. ACE inhibitors have the same remedial renal value as they do in other forms of hypertensive renal disease. Renal insufficiency varies in its pace of progression and may be retarded by control of hypertension, particularly by ACE inhibitors, and limiting protein intake, perhaps to 0.75 gm/kg. Following the creatinine clearance allows prognostication of time to ESRD. After creatinine has begun to rise, it falls by one-half every 36 months (31). The disease responds well to dialysis, and patients are candidates for renal transplantation.

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Neurology

Chapter 10

Neurology in Primary Care

*Cynthia G. Olsen and
Mark E. Clasen*

REVIEW OF PRINCIPLES OF NEUROLOGIC DISEASE

Upper and Lower Motor Neurons

Upper motor neuron lesions occur at any point from their origin in the motor cortex to the terminations of the neurons of the corticospinal tract in the synapses with dorsal horns or internuncial neurons. The latter occur at the levels of peripheral distribution of the motor pathway, synapsing with the lower motor neurons of the anterior horn cells. Except for symptoms owing to certain cranial nerve distributions above the decussation of the corticospinal tracts in the pyramids of the medulla, signs and symptoms of corticospinal tract lesions occur contralateral to the lesion. These include muscle weakness and/or paralysis; increased tendon reflexes; spasticity; little muscle atrophy; an extensor plantar response (Babinski), and loss of superficial abdominal and cremasteric reflexes.

Lower motor neuron lesions create: flaccid paralysis or muscle weakness; muscle wasting; loss of tendon reflexes; fasciculation over the affected musculature acutely, and preservation of normal plantar and abdominal reflexes.

Investigation of these systems may constitute the beginning neurologic evaluation, with other parts of the examination used to define more specifically the level and location of the lesion.

Diagnosis of Coma, Delirium, and Stupor

Coma is a state of unresponsiveness from which the patient can not be aroused. It results from a lesion in both cerebral hemispheres and/or the reticular activating system in the brainstem above the mid-pons. It is caused by structural lesions, metabolic disturbances, subarachnoid hemorrhage, meningoencephalitis, or seizures. Delirium is the presence of a fluctuating mental status examination that may be accompanied by autonomic disturbances, hallucinations, and motor disturbances. The term *stupor* usually means that a patient can be aroused only by use of painful stimuli. These stimuli may or may not elicit a verbal groan, and some avoidance posture may be attempted. Terms such as *stupor*, *obtundation*, and *semi-coma* fall in between coma and the state of being fully alert, awake, and aware. Confusional states, characterized by inattentiveness or a lack of thought clarity, fall into the delirium terminology. Despite these terms and their ambiguity, it is best to describe what is observed on physical examination to fully assess the neurologic diagnosis. After traumatic head injuries, the Glasgow scale may be used to predict the prognosis. (Table 10.1)

Specific Tests

Caloric testing (oculovestibular stimulation) is performed by irrigating the nonperforated tympanic membrane with 1 cc of ice water. In comatose patients who have an intact brainstem, the eyes deviate toward the side of caloric stimulation. Bilateral irrigation causes tonic downward deviation; if bilateral irrigation is performed using hot water, upward eye deviation is observed. No response to caloric stimulation using large volumes of water (≥ 50 ml) is indicative of peripheral vestibular disease, a structural lesion in the posterior fossa, or intoxication with sedative drugs. If partial eye responses are observed, or if internuclear ophthalmoplegia (medial longitudinal fasciculus lesion) is noted,

Table 10.1.
Glasgow coma scale.

Activity	Scale ^a
Verbal response	
None	1
Incomprehensible sounds	2
Inappropriate words	3
Confused	4
Oriented	5
Eye opening	
None	1
To pain	2
To speech	3
Spontaneously	4
Motor response	
None	1
Abnormal extensor	2
Abnormal flexor	3
Withdraws	4
Localizes	5
Obeys	6

Total score = sum of the score for each of the three components; score for a fully oriented alert patient = 15; score for a mute immobile patient with no eye opening = 3.
Reprinted with permission from Rowland LP, ed. Trauma, Merritt's Textbook of Neurology. 9th ed. Baltimore: Williams & Wilkins, 1995:442.

The anatomic pathways of cranial nerves III, IV, and VI are correlated with the findings of partial responses of the extraocular eye muscles.

APHASIA

This is an impairment of language produced by brain dysfunction. Nonfluent aphasia like Broca's aphasia are characterized by paucity of speech, effortful speech, dysarthria, and agrammatism, with preserved information content. Global aphasia is similar, but content comprehension is not preserved. A Wernicke's aphasia, on the other hand, has a fluent speech pattern of normal articulation and effort, but it is filled with empty content with little information. Fluent aphasia are associated with lesions in the left cerebral hemisphere, posterior to the Rolandic fissure, and nonfluent aphasia are associated with lesions in the same hemisphere anterior to the Rolandic fissure. More detailed testing to

distinguish among the dozen or so aphasic syndromes probes fluent or nonfluent speech, reading, writing, naming, and repetition abilities. Other disturbances of speech such as aprosody (loss of affective intonation, cadence, rhythm, and inflection of speech) can be either expressive or receptive. An expressive aprosody is produced by right frontal lobe lesions, whereas a receptive aprosody involves lesions in the right posterior temporal region.

Personality changes, such as the patient who becomes anti-social, makes remarks of a lewd nature, and/or displays inappropriate jocularity and generally who displays poor judgment may be suffering from orbitofrontal lobe lesions. This may occur with an otherwise intact neurologic examination. Apathy, on the other hand, may be a clue to medial frontal lobe lesions.

The so-called primitive reflexes (glabellar, palmomentary, suck, grasp), often associated with states of delirium, may be released (activated) by frontal lobe disinhibition and are likewise seen in the various pathologic conditions associated with dementias. In conclusion, the mental status, behavioral, and neurologic examination can help the clinician identify lesion location. Special testing and neurobehavioral syndrome patterns can likewise assist in making a diagnosis.

DEGENERATIVE DISEASES OF THE CNS

Multiple Sclerosis (MS)

MS is the greatest nontraumatic cause of neurologic disability in young adults. It typically affects those between 20 and 40 years of age and its prevalence is estimated at 400,000 in the United States. MS is a demyelinating disease of the CNS and is highly variable in course. A diagnosis of *definite* MS requires documentation of lesions that have occurred on more than one occasion and in more than one site with no other explanation. The diagnosis is often difficult and requires careful clinical observation. The etiology is unknown but may involve an infection and subsequent autoimmune process. MS may include sensory, visual, and motor dysfunction.

Active

These constitute 25% of cases and have a dysfunction that progresses rapidly over weeks to months, has a relapsing/remitting pattern, and can be terminal within months.

Progressive

These comprise 15% of cases and are classified as *chronic progressive*, as they progressively worsen after the onset without well-defined remissions and relapses. *Chronic relapsing* makes up 40% and develops a relapsing progressive course.

Benign

Twenty percent have few exacerbations and have a mild course with complete recovery with no marked impairment in function. The initial symptoms are primarily visual and sensory.

Diagnosis

The clinical presentation varies widely and depends on the site of demyelinating lesions. Monocular blindness, gait disturbance, and sensory changes are the most common symptoms. Retrobulbar optic neuritis with visual loss (central) and eye pain on movement occurs in 40% of patients. Corticospinal and sensory tract involvement are manifested as upper motor neuron spasticity, paresthesia, and pseudobulbar palsy. Cerebellar lesions produce dysarthria, staggering gait (titubation), intention tremor, and gait ataxia. Internuclear ophthalmoplegia results from a lesion of the medial longitudinal fasciculus and presents clinically when on lateral upward gaze, the abducting eye develops nystagmus, and incomplete adduction of the opposite eye occurs. Other brainstem symptoms include diplopia, trigeminal neuralgia, and nystagmus. Spinal cord involvement includes transverse myelitis and bladder dysfunction. Psychiatric manifestations, such as depression, are common.

Laboratory Testing

Magnetic resonance imaging (MRI) has greatly improved the diagnosis of MS and has a sensitivity of 90% to 97%. The disease is characterized by plaques in the white matter (90%) and spinal cord (30% to 40%). Plaques generally localize in the periventricular and callosal areas. Gadolinium enhancement can help differentiate between acute and chronic lesions. MRI may be useful in monitoring the course of illness and finding new asymptomatic lesions. Electrophysiologic studies (EPS) have been used to demonstrate the presence of lesions. Cerebrospinal fluid (CSF)

may be helpful if an elevation of immunoglobulin (70%) occurs, but does not exclude MS in its absence. MRI findings do not necessarily correlate with EPS or CSF findings. Blood chemistries, serologies, and hematologic studies are normal.

Treatment

The goals of treatment include continuity of care, management of symptoms, enhancement of personal freedom, autonomy in the face of disability, and emotional support. All patients deserve as much education about MS as possible and referral to a support group (National Multiple Sclerosis Society, 1-800-344-4867). Increased temperatures may block conduction in damaged nerve fibers, and patients should be told to avoid heat, e.g., spas. Exercise programs should be developed according to the patient's needs. Referral to a multidisciplinary team in a rehabilitation department should be considered. Physical therapy can improve muscle weakness and teach the most effective use of muscles. Ambulation disorders may require assistive devices. Spasticity can be controlled with range of motion (ROM) exercises and stretching; antispasm medications, such as baclofen and diazepam, are appropriate in moderate to severe cases. Tremor, often quite disabling, may be improved with a beta-blocker. Bladder control problems are often caused by detrusor instability. A bladder emptying program with prompted voidings, self-catherization and anticholinergic medications (oxybutin) are useful. An alpha-blocking agent may be called for if the urinary sphincter is unable to relax. Fatigue is common and can be controlled by regular exercise, conditioning and pacing one's activities. Work, sexual dysfunction, and mood disorder should be discussed. Drugs used for immunomodulation in MS include cyclophosphamide, azathioprine, cyclosporine, and beta-interferon. Trials with claberdine and methotrexate are underway.

Cyclophosphamide may be given with methylprednisolone in monthly intravenous doses. This combination appears to be helpful in patients under age 40. Beta-interferon (Betaseron) has been approved by the FDA for fully ambulatory patients with certain types of exacerbations. Beta-1A interferon, in particular, has been shown to reduce the number of exacerbations by 50%/year, reduce rate of progression, and reduce the number of brain lesions seen on MRI (1). Side effects include leukemia and ele-

ation of liver enzymes. These should be checked every month for the first 3 months, then every 3 months. Patients should be observed for depression and for possibility of suicide. Azothioprine and methotrexate are showing promise at present (2).

Dementia

Alzheimers disease and other progressive dementias affect global cognitive functioning, are severely disabling, and typically affect the elderly. However, cases are found as early as the third and fourth decades of life. The purpose of a work-up in dementia is to detect reversible causes of cognitive impairment, evaluate the patient's other medical and social needs, and determine caregiver status.

Differential Diagnosis

Alzheimer's dementia is the most common form and involves impairment in abstract thinking, poor judgment, higher cortical dysfunction, and personality change. These disturbances significantly interfere with social and personal activities and are not a part of delirium. The onset is insidious but gradual, progressive, and short-term memory is impaired. Multi-infarct dementia is caused by repeated, small strokes and is commonly found in patients with hypertension, diabetes, and atherosclerotic heart disease. The onset and progression is in a step-wise manner with defined episodes of worsening. Approximately 15% of patients have a combination of these two dementias. Other causes of dementia to be ruled out include neoplasia, infections, toxic and metabolic disorders, hereditary causes, pseudodementia (depression) and trauma, i.e., subdural hematoma or normal-pressure hydrocephalus.

Clinical Evaluation

A thorough history focusing on chronology of symptoms and impairment, changes in mood and behavior, physical changes, and medical history is essential. An attempt at weaning all unnecessary medications, especially those with anti-cholinergic side effects, is prudent. A complete physical examination with attention to mental status, cardiovascular, and neurologic exam should be performed. Sensory impairment should be sought and corrected. Interview of the caregiver or family often reveals information not obtainable from the patient.

Laboratory Testing

A dementia evaluation should include the following for determination of comorbid conditions or reversible causes: serum chemistry, syphilis serology, thyroid function tests, complete blood count with indices, serum vitamin B12 and red blood cell folate determination, erythrocyte sedimentation rate, and urinalysis. CNS imaging with MRI or CT scan of the brain is beneficial and should be strongly considered. Further testing should be based on the history and physical and may include CSF studies, human immunodeficiency virus screening, screening for heavy metal, electroencephalogram (EEG), electrocardiogram (EKG), screening for drugs of abuse, and neuropsychological testing.

Treatment and Management

The diagnosis of Alzheimer's or other progressive dementing illness can be devastating to the patient and family. Continuity of care and quality of life is the primary-care physician's foremost goal. Treatment should be directed at remediable causes and contributors to confusion, such as hypothyroidism, sensory impairment, and social isolation. Patients should be informed of their illness early so that they may prepare advanced directives such as living wills and durable power of attorney. Fifty percent of dementia patients suffer from concurrent depression and benefit from antidepressant therapy. Doses of antidepressant should be started low and gradually tapered upward. These patients are usually sensitive to anticholinergic side effects; antidepressants appropriate for this group include nortriptyline 25 to 75 mg q h s and paroxetine 10 to 30 mg every day. Behavioral disturbances are often disruptive and can lead to institutionalization. Participants of change in behavior include arthritic pain, urinary tract infection, and change in environment. Anxiety and worry can be controlled with buspirone hydrochloride (5 to 10 mg three times a day) and low-dose benzodiazepines (lorazepam 0.25 to 1.0 mg twice a day). Aggressive and psychotic symptoms can be controlled with low-dose antipsychotics (haloperidol 0.5 to 1.0 mgs q h s). "Sundowning," or evening confusion, can be relieved with reassurance and trazadone (25 to 50 mg) if necessary. Both physical and chemical restraints have been shown to increase injury in this group and should be used only if the demented person is at serious risk to himself or others should be monitored closely,

and discontinued as soon as possible. Tacrine has shown some benefit in reducing confusion in elderly Alzheimer's patients with mild to moderate impairment; this treatment requires weekly monitoring of SGOT and is associated with gastrointestinal upset. The long-term benefit of this drug has not been established. Family and caregivers benefit from supportive counseling and education (Alzheimer's Association, 1-312-853-3060).

Parkinson's Disease

Parkinson's disease is a progressive CNS disorder affecting 1% of people over 60 years. Loss of nigrostriatal dopamine results in the characteristic motor findings of Parkinson's, and replacement of cerebral dopamine reverses these symptoms.

Clinical Findings

Cardinal symptoms of this illness include tremor, bradykinesia (slowness), gait disturbance, muscle rigidity, and postural instability. Presence of all manifestations are unusual in early disease and may make diagnosis difficult. Other findings include mask-like faces, psychomotor retardation, fatigue, sleep disorder, and unilateral findings. This presentation may lead to the misdiagnosis of depression or stroke. Fifty percent of tremor patients do not have Parkinson's, and a broader differential diagnosis needs to be considered. History should focus on the development of neurologic symptoms, depression, other concurrent medical illnesses such as hypothyroidism, medications, and injuries such as falls. Drug-induced Parkinson's should be ruled out by the elimination of offending drugs, such as neuroleptics, antiemetics, metoclopramide, and the antihypertensives reserpine and methyldopa. Physical examination should include thorough mental status and neurologic exam. The tremor found is typically slow and coarse, initially unilateral, and resting, and often a pill-rolling movement of the thumb and fingers are noted. Passive movement of the wrist or elbow may reveal cog-wheeling rigidity. The gait features shuffling, lack of arm swing, and turning of the body en bloc. Speech is often soft, monotonal, and may be inaudible. Autonomic insufficiency may result in constipation, impotence, and orthostatic hypotension. Mental changes, such as dementia, occur in about 15% to 20% of people with Parkinson's.

Treatment

Care of the Parkinson's patient should focus on proper diagnosis, maintenance of neuromuscular function, and reduction of complications such as falls. A rehabilitation referral can be beneficial to the patient with gait problems and in the recommendation of assistive devices. Reduction of anxiety and depression is important, and a psychotherapy referral may be considered. An early exercise program may reduce disability. Support groups for patients and family are available (American Parkinson's Disease Association, 1-800-223-APDA). Carbidopa-levodopa (Sinemet) remains the foundation of treatment and should be started in small dosages and titrated to the lowest effective amount (25/100 tablet three times a day one hour before meals). Seregiline therapy may slow the progression of disease (5 mg twice a day) and potentiate the effect of levodopa. However, it is expensive, and consideration should prompt a neurology consultation. Tremor may also be controlled with anti-cholinergic drugs such as diphenhydramine (Benadryl), benzotropine mesylate (Cogentin), or trihexyphenidyl HCl (Artane). Amantidine HCl (Symmetrel) may temporarily improve rigidity and bradykinesia. Half of these patients experience depression and may benefit from an anti-cholinergic antidepressant such as amitriptyline (Elavil) or imipramine (Tofranil). Conversely, the clinician should remember that the elderly are highly susceptible to anti-cholinergic side effects, and dementia may be precipitated.

SEIZURE DISORDERS

Seizures are classified as generalized or partial. Generalized seizures are the tonic-clonic seizing observed in grand mal events. Absence seizures and "other" types of seizures are also considered generalized seizure disorders. Partial seizures are divided into simple and complex partial seizures.

Status epilepticus is a state in which seizures don't relent or occur so frequently that full consciousness is not regained. This is an emergency that, if untreated, may result in brain damage or death.

Treatment

Various Protocols

A fairly standard protocol among many commences with diazepam (Vallium) 10 mg intravenous push over a period of 2 minutes. Respiratory depression and/or hypotension is the primary caution; thus, ventilation preparedness is required. Since

seizuring recurs or continues 50% of the time, a maintenance phenytoin drip is usually commenced. This is usually 1000 to 1500 mg mixed in a NON-dextrose solution (18 mg/kg), and given at a rate not to exceed 50 mg/minute. If seizing continues after the total body dose is given, a paraldehyde drip may be used or general anesthesia required.

The following agents are commonly used for control of generalized tonic-clonic and partial seizures: phenytoin, carbamazepine, phenobarbital, and mysoline (usually a second-line agent). Valproic acid and ethosuximide are used for absence seizures, and klonopin is used for control of myoclonic seizures. Single and multiple drug regimens are often required for seizure prevention, and most anticonvulsant drugs require therapeutic level monitoring; some require serum chemistry and blood count surveillance. All require alertness to side effect profiles of each agent.

PERIPHERAL NERVE SYNDROMES

The Differential Diagnosis in Peripheral Neuropathies is Considerable

Hereditary etiologies can be delineated from the family history; drugs and toxins from past medical and social histories, and neoplastic, vasculitic, infectious, inflammatory, and metabolic causes from the history, physical examination, and lab.

History and physical examination is the best method to distinguish among this considerable list. A useful approach is to distinguish whether or not a single nerve is involved, and whether the involvement is motor, sensory, autonomic, or combinations of the three.

Guillain-Barré syndrome is an example of polyneuropathy that is predominantly manifested by motor weakness that begins in the legs, and ascends in the cephalad direction. To a lesser extent sensory impairment may accompany this entity, and autonomic involvement becomes common, often leading to cardiorespiratory collapse. Certain shellfish contain saxitoxin, a sodium channel blocker, which may deplete the action potentials of nerves and muscles. A rapidly progressing ascending sensory loss followed by motor paralysis is the clinical picture of this shellfish poisoning. No antidote is available, but mechanical ventilation and support of blood pressure, and enemas to remove the toxin results in most patients recovering from this bizarre entity. Tick paralysis is another neurologic manifestation of certain tick bites. Bell's palsy is a classic example of pathology along the peripheral branch of the facial

nerve. Not only can the motor innervations of this nerve be disrupted, but also it may be accompanied by taste disruption, hyperacusis, and lacrimation. Weakness in the intrinsic muscles of the hand may be the clue to the cervical rib syndrome; peripheral sensory losses in the extremities may reveal underlying diabetes or alcoholism. Dermatomal paresthesias indicate specific nerve root(s) being compressed in lumbar disc disease.

Laboratory Testing

Nerve conduction velocity studies (NCV) are useful when a clearer definition of nerve functioning is needed. In carpal tunnel syndrome, nerve conduction velocities are decreased between the arm and hand because of the nerve compression of the median nerve at the carpal tunnel (Chapter 23). Nerves that are compressed, metabolically starved, injured by trauma or toxin, or damaged immunologically conduct at the slower rate. Thus, heavy metal screening is sometimes a necessary part of the evaluation.

EMG studies help evaluate muscles and their responses to their nerve supplies. Complete transection of a nerve supplying a muscle's motor end plates results in denervation muscle fasciculations on the EMG. Partial denervation patterns are likewise appreciated on this type of testing. EMGs are useful in looking at the health of the nerve supplying each muscle group. Primary muscle pathology is diagnosed by biopsy and certain chemistries.

SYNCOPE

Syncope is a sudden temporary loss of consciousness associated with a loss of postural tone. Falls related to syncope may result in serious trauma such as head injury and fracture, especially in the elderly. In most cases it results from a reduction of cerebral blood flow. Presyncope is a sensation of faintness. Vertigo is a sensation of false movement, either rotational or linear (Chapter 1). The term *drop attack* refers to loss of tone leading to a fall without the loss of consciousness. The work-up of syncope should be guided by careful history and physical examination.

Differential Diagnosis

The majority of cases are because of noncardiac causes that enhance susceptibility to vasovagal and orthostatic mechanisms such

as drug use, alcohol abuse, hypoglycemia, hypoxia, hyperventilation, acute and chronic blood loss, volume depletion, hyperthermia, and pain. Emotional shock and panic may cause syncope through vasovagal bradycardia, neurogenic loss of arteriolar tone, and hyperventilation. Visceral precipitants that stimulate vasovagal responses include cough, defecation, micturition, and swallow syncope. These etiologies can be determined by a detailed history of the events surrounding the episodes. Seizures, cerebrovascular disease, and cardiac causes are serious causes that require further diagnostic testing. Associated symptoms such as incontinence, aura, mouth biting, headache, postictal state, chest pain, dyspnea, palpitations, and confusion help guide the work-up. Patients with comorbid disease are at higher risk for serious causes of syncope.

Physical Examination

The examination should concentrate on the neurologic and cardiovascular status of the patient. Careful attention to dysrhythmia, heart murmur, and focal neurologic findings is important. Measurement of vital signs include blood pressure in both arms. An office tilt test is worthwhile. The patient should be supine for at least 5 to 10 minutes, and BP and pulse determined. The patient should then sit up with a repeat vital sign measurement, and then stand with repeat measurements for up to 5 minutes to uncover any delayed orthostatic response. A drop of more than 20 mm Hg in systolic pressure or 10 mm Hg diastolic pressure suggests orthostatic hypotension. Determination of the EKG R-R interval in the office can be performed while the patient breathes slowly. Loss of variation demonstrates autonomic dysfunction often seen in diabetes mellitus and Parkinson's disease.

Diagnostic Testing

Basic blood chemistry, blood count, and urinalysis should be performed to rule out metabolic disorders, infectious causes and anemia. An EKG may uncover underlying heart disease but rarely detects dysrhythmia and thus a 24-hour Holter monitor should be performed. Cardiac outflow obstruction, as in aortic stenosis, may be fatal and requires an echocardiogram for detection. Electroencephalogram should be considered if the history suggests seizures or undetermined central nervous system disease (CNS). Other CNS etiologies of syncope, such as transient ischemic attacks, stroke, migraines, and subclavian steal should be sought

for with CNS imaging, cerebral flow studies and angiography. The latter should be reserved for serious situations not otherwise elucidated. Cervical spinal stenosis is suggested in patients with drop attacks and previous neck injury or osteoarthritis and is diagnosed by magnetic resonance imaging (MRI) of the neck.

Treatment and Management

Discontinuation of all unnecessary medication and alcohol and avoidance of offending situations, e.g., extreme heat, in situational syncope is simple and beneficial. Treatment is then based on the etiologic cause of the syncope and management of disease states. Reduction in hypertensive medication, elastic hosiery, and leg flexion is helpful in various cases. Neurology or cardiology consultation for the serious causes of syncope is appropriate.

BRAIN DEATH

A standard procedure for determining brain death includes the following criteria: prerequisite conditions, clinical examination confirmation, sufficient time for evaluation to determine irreversibility, and confirmatory testing. The medical record should include the following: etiology and irreversibility of the condition, the neurologic examination findings noted by date and time of day, determination of apnea, reason for and result of confirmatory test(s), and the repeat, after an appropriate interval, of the neurologic examination with results documented.

Prerequisite conditions are those that are known to cause irreversible brain injury and include significant toxic or metabolic disturbances known to be incompatible with recovery. In the evaluation of these irreversible causes, the core body temperature must be greater than 32°C or 90°F. The clinical neurologic examination findings that confirm brain death include apnea (by a formal apnea test if no medical contraindication), absence of brainstem reflexes, and coma with absence of nonspinal motor responses.

Depending upon the clinical situation, at least 2 to 24 hours at a minimum are required to determine the irreversibility of the condition. Severe facial trauma, pre-existing pupillary abnormalities, toxic levels of sedating drugs or drugs that alter neurologic examinations, sleep apnea, or severe chronic obstructive pulmonary disease may interfere with the clinical diagnosis of brain

death. In this setting, confirmatory laboratory tests are recommended. These tests may include conventional angiography, electroencephalography, transcranial Doppler ultrasonography, cerebral radionuclide angiogram, and somatosensory evoked potentials.

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Diseases of the Respiratory Tract

Chapter 11

Pneumonias, Bronchitides, and Chronic Lung Disease

*Martin S. Lipsky and
Marna Sternbach*

PNEUMONIA

Pneumonia is one of the most common infectious diseases seen in family practice and the sixth leading cause of death in the United States. Each year more than 3 million Americans will develop pneumonia, making it the 25th most common problem treated by generalists.

The diagnosis of pneumonia is based on clinical history, physical examination, and chest x-ray findings. Clinical features that suggest pneumonia are fever combined with respiratory complaints such as cough, sputum production, chest pain, and shortness of breath. Although most patients have one or more of

these symptoms, mental confusion may be the sole presenting symptom in elderly or debilitated patients. Physical findings include fever, tachycardia, tachypnea, and rales. More specific, but less common on examination, are signs of lung consolidation such as bronchophony, dullness to percussion, and egophony.

A chest film showing infiltrates is usually required to establish the diagnosis. False negative films are rare, but can be found in patients with pneumonia who have dehydration, incipient infection, or profound neutropenia, and in 10% to 30% of patients with *Pneumocystis carinii* pneumonia (1).

Although differentiating pneumonia from bronchitis may require a chest x-ray, the prevalence of pneumonia among adults with an acute cough is only about 3%. Therefore, radiologic evaluation should generally be reserved for patients with suggestive histories and findings on physical examination (2). In otherwise healthy adults, an entirely normal pulmonary examination excludes pneumonia 95% of the time. Clinical findings are less reliable in HIV-infected patients, debilitated individuals, and in patients with underlying disorders such as chronic lung or heart disease. Therefore, the threshold for obtaining chest x-rays in these types of patients should be lower.

Besides confirming the presence of pneumonia, a chest film provides other useful information. First, the pattern of the infiltrate may suggest the etiology. Consolidation or a lobar infiltrate suggests a bacterial pneumonia, while a diffuse patchy infiltrate is more consistent with a viral, mycoplasmal, or chlamydial infection. Unfortunately, considerable overlap exists in x-ray findings, and neither pattern is diagnostic. Chest films also help assess the extent of the pneumonia (e.g., multilobar versus limited infiltrate) and can detect the presence of pleural effusions. Small pleural effusions (layering less than 2 cm on a lateral decubitus film) in a nontoxic patient responding to antibiotic therapy may not need thoracentesis. However, thoracentesis is mandatory for larger effusions or in sicker patients. Finally, chest films may suggest an alternative diagnosis, such as lung abscess, tumor, or tuberculosis.

Etiology

The causes differ depending on the treatment setting and the patient's age. In healthy adults, the causes of community-acquired pneumonia in the probable descending order of frequency are *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, *Haemo-*

philus influenzae, respiratory viruses, Chlamydia pneumoniae, and Moraxella catarrhalis. An etiologic agent cannot be identified in 30% to 50% of patients (3). In older patients, or in patients with comorbidities, pathogens such as Mycobacterium tuberculosis, Staphylococcus aureus, Gram-negative bacilli, anaerobes, and Legionella must also be considered.

Streptococcal pneumonia

In nearly all studies, S. pneumoniae is still the most common cause of community-acquired pneumonia in patients requiring hospitalization. Classically, pneumococcal pneumonia presents acutely with rigors and rust-colored sputum. The sensitivity of a sputum gram stain for pneumococci ranges from 15% to 60%. When lancet-shaped, Gram-positive diplococci are present, the positive predictive value is 80% to 90%. Penicillin remains the treatment of choice; erythromycin is an acceptable alternative. In geographic areas with high rates of penicillin-resistant pneumococci, ceftriaxone and vancomycin are alternatives to penicillin.

Mycoplasma pneumonia

Mycoplasma pneumonia most commonly affects adolescents and young adults. Although mycoplasma pneumonia usually causes prominent pulmonary symptoms, it should be viewed as a systemic illness. In contrast to pneumococcal pneumonia, the onset of mycoplasma is usually gradual, with a dry, nonproductive cough. Extra-pulmonary manifestations, such as headache, fever, malaise, upper respiratory symptoms, and diarrhea, are often present. The absence of severe myalgias helps to distinguish mycoplasma from viral pneumonia.

Cold agglutinin titers are elevated in 75% of patients. Although not specific for mycoplasmal infection, titers above 1:64 in the appropriate clinical setting suggest mycoplasmal infection. Alternatively, elevated IgM antibodies to mycoplasma usually indicate active disease. Erythromycin and tetracyclines are the antibiotics of choice, and are given for 10 to 14 days. Antibiotic treatment of mycoplasmal pneumonia is most effective if prescribed early in the clinical course.

Legionella

Legionella presents clinically and radiologically as an atypical pneumonia. Although it may present as a fulminant illness, the

onset is usually gradual. Clinical clues that suggest *Legionella* are extra-pulmonary features such as a relative bradycardia, mental status changes, abdominal pain, and diarrhea. Ear pain, sore throat, or rash suggest a cause other than *Legionella*.

Laboratory findings that point to *Legionella* include abnormal liver function tests, hyponatremia, and hypophosphatemia. A positive direct sputum immunofluorescent antibody stain or the presence of *Legionella* antigen in the urine confirms the diagnosis. Although not diagnostic, a *Legionella* titer $>1:264$ in a patient with appropriate clinical features suggests *Legionella* infection.

Legionella should also be considered in patients with rapidly progressive asymmetrical infiltrates. A 14- to 21-day course of erythromycin is the preferred treatment. Azithromycin or clarithromycin are also effective macrolide antibiotics that are frequently better tolerated but are more expensive. Doxycycline and the fluoroquinolones are also effective antibiotics.

Bacterial Pneumonias

Bacterial agents other than *S. pneumoniae* that cause pneumonia include *H. influenzae*, *M. catarrhalis*, and *Klebsiella pneumoniae*. Cigarette smoking, advanced age, and chronic bronchitis are factors associated with *H. influenzae* and *M. catarrhalis* infections. Alcoholic patients and debilitated patients are at risk for *K. pneumoniae*. *S. aureus* pneumonia is often preceded by an influenza infection. Gram-negative bacilli rarely cause community-acquired pneumonia, but should be considered in hospital and nursing home patients with pneumonia. Failure to detect *S. aureus* or Gram-negative bacilli in a pretreatment sputum suggests that these organisms are unlikely causes of the illness. Anaerobic infections should be considered in patients at risk for aspiration. Although the length of therapy is variable, most practitioners treat the common bacterial pneumonias for 10 days.

Viral Pneumonias

Patients with viral pneumonia are usually less toxic, have either a dry cough or minimal sputum production, and often present with myalgias as a prominent feature. Most commonly influenza virus and less commonly parainfluenza and adenovirus cause viral pneumonia (1). Epidemiologic patterns may be helpful to identify influenza infections. Patchy infiltrates and a WBC $<15,000$ are also

more typical of viral pneumonias. Sometimes, a specific viral infection such as chickenpox is evident from its extra-pulmonary features. Influenza pneumonia may benefit from treatment with amantadine (2).

Approach to Community-Acquired Pneumonia

The two major issues to address in an ambulatory patient with pneumonia are: Can this patient be treated safely as an outpatient? and What is the best antibiotic therapy?

Although no absolute guidelines are available, certain factors identify patients at risk for a complicated course and predict the need for admission. These guidelines are based on patient characteristics, clinical findings, laboratory results, and the suspected organism. Older patients with underlying comorbid conditions such as heart or lung disease, diabetes, renal failure, malignancy, alcoholism, or HIV and other immunosuppressed states generally require inpatient treatment. Likewise, patients who cannot tolerate oral antibiotics, or appear toxic with respiratory distress or hypotension also merit inpatient treatment. Laboratory abnormalities such as leukopenia (<4000), anemia, leukocytosis ($>25,000$), hypoxemia, ($\text{PaO}_2 <60$), or evidence of an infection with a virulent organism such as *S. aureus*, *Legionella*, or a Gram-negative bacillus predict the need for hospitalization. Chest x-ray abnormalities such as pleural effusions, cavitary lesions or multilobar infection also suggest the need for admission.

Treatment decisions should be based on the most likely offending organisms. If available, gram stain results should guide therapy, although they need to be interpreted in conjunction with the clinical picture. Frequently gram staining is difficult or impractical to obtain in the outpatient setting, leading physicians to initiate therapy empirically based on the most likely cause. A detailed history, including travel history, animal exposure, occupational history, and HIV status, helps to eliminate less common causes of pneumonia. For young adults treated as outpatients, erythromycin or one of the newer better-tolerated macrolides, such as clarithromycin or azithromycin, are good choices for empiric antibiotic therapy. The newer macrolide antibiotics cover both *S. pneumoniae* and the atypical pneumonias caused by *Mycoplasma*, *Legionella*, and *Chlamydia*. An alternative is doxycycline, although 10% to 20% of pneumococci may be resistant to tetracyclines (1).

For patients 60 and over and for those with coexisting illnesses, trimethoprim-sulfamethoxazole or a second-generation oral cephalosporin is a reasonable choice. Alternatives include amoxicillin, amoxicillin-clavulanic acid, and extended spectrum macrolides. Dosages of commonly used outpatient antibiotics are listed in Table 11.1.

Most patients with appropriate treatment will start to improve within 72 hours. Patients who worsen or fail to improve on outpatient therapy should be considered for hospitalization and a more extensive work-up.

The need for follow-up chest films is controversial, but most authorities recommend that smokers or patients older than 40

Table 11.1.
Outpatient drugs for pneumonia.

Antimicrobial agent	Dose	Comment
Amoxicillin	250–500 mg 3×/day	Inexpensive, increasing resistance
Amoxicillin-clavulanate	500 mg/125 mg 3 ×/day	High incidence of diarrhea
Azithromycin	500 mg/day 1, then 250 mg/day	GI side effects
Cefuroxime	250 mg 2×/day	Hypersensitivity reactions, diarrhea
Ciprofloxacin	500–750 mg 2×/day	Expensive, less active against <i>S. pneumoniae</i>
Clarithromycin	250–500 mg 2×/day	Active against <i>H. influenzae</i> , GI effects, abnormal taste
Doxycycline	200 mg/day 1, then 100 mg 2×/day	Photosensitivity reaction
Erythromycin	250–500 mg 4×/day	High incidence GI effects, poor <i>H. influenzae</i> activity
Ofloxacin	400 mg 2×/day	Better <i>S. pneumoniae</i> coverage than ciprofloxacin
Penicillin	500 mg 4×/day	Increasing <i>S. pneumoniae</i> resistance
Tetracycline	500 mg 4×/day	Photosensitivity reactions
Trimethoprim-sulfamethoxazole	(160–800 mg) 1 pill 2×/day	Increased dosage needed for <i>pneumocystis carinii</i>

years old should have a repeat chest x-ray. Infiltrates that fail to improve at all after 4 weeks or to resolve by 12 weeks need further evaluation to rule out uncommon pathogens, an underlying malignancy, or a noninfectious disease process.

Recommendations for an initial evaluation of inpatients with pneumonia include chest x-ray, ABG, CBC, chemistry profile, 2 to 3 blood cultures, HIV testing (for patients 15 to 54), sputum gram stain and culture, direct fluorescent antibody test, *Legionella* testing (e.g., serology, DFA sputum culture, urinary antigen), and mycoplasma—IgM antibodies (1). Initial therapy should be based on the clinical presentation and gram stain results if available. Recommended empiric antibiotic regimens vary, but many authorities recommend a second- or third-generation cephalosporin with the addition of a macrolide in geographic areas of high prevalence for atypical pneumonia or if clinical features suggest an atypical pneumonia. Critically ill patients with pneumonia or those with underlying risk factors should have broad spectrum antibiotic coverage with a third-generation cephalosporin, a macrolide, and possibly an aminoglycoside.

PLEURITIC CONDITIONS

Pleural inflammation can produce pleuritic pain, characterized by stabbing pain induced by respiration. The most common causes of acute pleuritic pain are viral pleurisy, idiopathic pleuritis, pneumonia with pleuritis, bronchial asthma, and chest wall pain. Movement and palpation have little effect on pain from pleural inflammation, and if present suggest musculoskeletal chest pain. Other diseases such as neoplasm, uremia, and connective tissue disease can also cause pleural inflammation, effusion, and pleuritic pain.

Pleural Effusion

One manifestation of pleural disease is a pleural effusion. Normally the pleural space contains about 10 ml of serous fluid. An imbalance between hydrostatic and oncotic pressures can result in fluid accumulation, or a pleural effusion. Inflammation of the pleura or its adjacent structures can cause an exudative effusion. In contrast, increased hydrostatic pressure and/or decreased oncotic pressure produce transudates.

Congestive heart failure (CHF) is one of the most common

causes of a transudative effusion. Most CHF effusions are bilateral; unilateral effusions due to CHF are usually right-sided. Hypoalbuminemia as seen in nephrotic syndrome and cirrhosis, or fluid retention from renal failure can cause transudates. Transudative effusions after coronary bypass graft surgery are common and do not necessarily imply serious disease. Neoplasm is a relatively common and worrisome cause for an exudative effusion.

Pleurisy

• Viral infections are a common cause of pleuritic pain in the outpatient setting. Viral pleurisy is a self-limited infection especially common in children and young adults. Usually a typical viral prodrome is followed by pleuritic pain, often severe. Pneumonia can also cause pleuritic symptoms.

Differentiating patients with idiopathic pleurisy from those with pulmonary embolism may be difficult. Predisposing factors such as bed rest, prior embolic disease, cancer, or recent surgery increase the risk for pulmonary embolus. Although radiographs are usually normal in patients with pulmonary embolus, a wedge-shaped infiltrate or a pleural effusion is unusual in viral pleuritis and suggests embolic disease. Associated symptoms or findings such as marked shortness of breath, hemoptysis, or clinical evidence of thrombophlebitis make it essential to exclude the diagnosis of pulmonary embolism. Perfusion lung scanning is a good initial test, since a normal perfusion scan virtually excludes the diagnosis of a pulmonary embolism. Abnormal perfusion scans in patients with acute pleuritic pain merit further testing.

Diagnosis of Pleural Effusion

A chest film can confirm the presence of an effusion and can suggest the cause. For example, hilar adenopathy, a lung mass, or radiologic signs of CHF may point to a specific etiology. Sometimes a pleural effusion with a clinically evident cause may be treated and followed expectantly with serial chest x-rays.

Thoracentesis is indicated when the cause of the pleural effusion is uncertain, for symptomatic effusions, for persistent effusions despite therapy, or in cases of suspected neoplasm or empyema.

A thoracentesis can be performed safely if at least one cm of fluid layers out on a lateral decubitus film. Loculated or very small effusions may need tapping under ultrasound or CT guidance.

Table 11.2.
Pleural fluid analysis.

Cell Count and Differential	Bloody fluid suggests cancer, pulmonary infarction, trauma, and tuberculosis. Lymphocyte predominance (>50%) is common in lymphoma and tuberculosis.
Gram Stain and Culture	Useful to diagnose infections. Special cultures/stains for suspected mycobacterial disease or fungal infection.
Cytology	Positive in about 60% of malignant effusions.
pH	Lower in rheumatoid disease, parapneumonic effusions.
Glucose	Lower in RA, parapneumonic effusions, TB.
Amylase	Elevated levels suggest pancreatitis.

Pleural fluid analysis differentiates a transudate from an exudate. Any one of the following classifies pleural fluid as an exudate: a) a pleural fluid protein to serum protein ratio greater than 0.5 or an absolute protein >3.0 gram/dL; b) a pleural fluid to serum LDH ratio greater than 0.6, or c) an absolute pleural fluid LDH >200 U/liter (4). Transudates are commonly caused by CHF, cirrhosis, and hypoalbuminemic states and generally require no further search for an etiology. Exudates have a much larger differential diagnosis and include infections, neoplasm, collagen vascular disease, drug reactions, and pulmonary infarction.

Additional tests that are helpful in analyzing pleural fluid are listed in Table 11.2.

Pleural Effusions and Pneumonias

Pneumonia, regardless of the etiologic agent, can cause a pleural effusion. A parapneumonic effusion is generally caused by inflammation and increased pleural capillary leakage. A parapneumonic effusion can be managed expectantly if the effusion is small and is responding to antibiotic therapy. Small parapneumonic effusions almost always resolve with appropriate antibiotic therapy (3). On the other hand, empyemas, i.e., grossly infected pleural fluid, require chest tube drainage. Complicated parapneumonic effusions are characterized by fibrinogenic fluid and may also need drainage. A positive gram stain, a pH <7.0, a glucose < 40 mg/dL, or a pH

of 7.0 to 7.2 with an LDH greater than 1000 IU predict the need for chest tube drainage of the pleural space.

CHRONIC OBSTRUCTIVE LUNG DISEASE (COPD)

COPD is characterized by irreversible airflow obstruction because of chronic bronchitis or emphysema. Chronic bronchitis is defined clinically as cough and sputum production for at least 3 months of the year for 2 consecutive years. Emphysema is an anatomic abnormality, defined as the destruction of alveolar walls resulting in dilation of terminal air spaces. Features of emphysema and chronic bronchitis are compared in Table 11.3. In practical terms, however, they should not be considered as isolated disorders, because most COPD patients have elements of both.

Experts estimate that as many as 15 million Americans have COPD, making it second only to arthritis as a cause of long-term disability and functional impairment. COPD is the fourth leading cause of death, and while the mortality from heart disease and stroke are declining, the death rate from COPD is increasing.

Smoking and age are the major risk factors for COPD. More than 90% of patients with COPD have a history of smoking. However, since not all patients with similar smoking histories have the same degree of pulmonary dysfunction, genetic factors must play

Table 11.3.
Clinical features of emphysema and bronchitis.

Characteristics	Emphysema	Bronchitis
Dyspnea	Relatively early	Relatively late
Sputum production	Scanty, mucoid	Copius, purulent
Cough	After dyspnea starts	Before dyspnea starts
CXR	Hyperinflation, small heart	Increased broncho-vascular markings
Hematocrit	Normal	May be increased
Spirometry		
FEV ₁ /FVC	Decreased	Decreased
TLC, RV	Markedly increased	Moderately increased
DLCO	Decreased	Normal
ABG		
Pa CO ₂	Normal (until late)	Increased
Pa O ₂	Normal (until late)	Decreased
COR Pulmonale	Rare	Common

role in disease development. Smoking initiates an inflammatory process by activating proteases in the respiratory tree. Alpha-1 antitrypsin is an antiprotease that inhibits the destructive capabilities of proteases. Smokers who develop COPD typically do so in their 50s with a smoking history of at least 20 pack years. Alpha-1 antitrypsin deficiency should be considered in nonsmokers developing COPD or in smokers who develop disease at an earlier age or out of proportion to their smoking history. Peripheral Alpha-1 antitrypsin is available for treatment, but its expense limits its use to patients with moderate airway obstruction, willingness to stop smoking, and antitrypsin levels <80 mg/dL. Since Alpha-1 antitrypsin therapy does not reverse lung disease, patients with severe COPD are not usually treated. Other factors that may contribute to developing COPD are air pollution, childhood respiratory illnesses, and occupational exposures.

Dyspnea is the most common presenting symptom and is often accompanied by cough, sputum production, and wheezing. Initially, the physical examination may be unremarkable. As the disease progresses, however, wheezing and bronchi may be present along with decreased breath sounds, flattened diaphragms, and hyperresonance to percussion. Patients with severe COPD may exhibit pursed lip breathing, and clinical signs of cor pulmonale, such as peripheral edema.

A chest x-ray is useful to evaluate patients with suspected COPD. Although a relatively insensitive test for diagnosing COPD, hyperinflation, flattened diaphragms, narrow cardiac silhouette, and increased retrosternal airspace are classic radiographic findings in advanced disease. Chest x-rays can also exclude other pulmonary diseases and detect the presence of an underlying lung cancer.

Spirometry should generally be performed as part of an initial evaluation and measures airflow obstruction. Airway obstruction is defined by a forced expiratory volume in one second/forced vital capacity (FEV1/FVC) ratio less than 75%. The severity of airflow limitation is based on the absolute value FEV1. Mortality correlates with a decrease in FEV1, and the 5- and 10-year survival rates for patients with COPD begin to decline markedly once the FEV1 falls to 1.25 liters.

Occasionally patients with an abnormal FEV1/FVC ratio have normal FEV1. This pattern represents early COPD with primarily small airway disease. In this case, the forced expiratory flow (FEF)

25 to 75 is decreased, and may be the first abnormality seen in COPD. This finding represents an ideal opportunity for a family physician to intervene by encouraging smoking cessation.

Significant arterial blood gas (ABG) abnormalities for patients with COPD are unusual until the FEV1 is less than 1.5 L. An FEV1 of less than 1.0 liter is associated with the presence of CO₂ retention. Indications for obtaining an ABG include initial assessment of a patient with moderate or severe disease, the presence of cor pulmonale, polycythemia, or dysrhythmias, preoperative evaluation, and initiation and/or monitoring of oxygen therapy. ABGs are also essential in patients suffering confusion or respiratory deterioration.

Therapy

The main goals of therapy are to alleviate symptoms and preserve pulmonary function. The single most important part of any treatment program is smoking cessation. For patients who can stop smoking, the rate of decline in FEV1 reduces to the rate seen in nonsmokers. Also important are minimizing environmental and occupational exposures, and using appropriate vaccines to prevent infection. Most experts recommend the use of annual influenza vaccination and pneumococcal vaccination in COPD patients.

The drugs in the following discussion are introduced in their descending order of priority and are used additively as need for therapy progresses. The quaternary anticholinergic, ipratropium bromide, is the inhaled drug of choice for COPD patients (5). The drug's effectiveness is similar to beta-agonists, but with fewer side effects. The dosage may be pushed up to 4 to 6 puffs, 4 times a day, before adding additional bronchodilators. Ipratropium has a more gradual onset of action but lasts longer than beta-agonists. For maximum effectiveness, ipratropium requires regular use.

Beta-agonists (e.g., albuterol), the recommended second-step drug, can supplement ipratropium in patients not experiencing adequate symptom relief. Side effects include tremor and palpitations. Inhalation is the preferred delivery method since a properly used metered dose inhaler (MDI) is as effective as oral beta-agonists and has fewer side effects. Training patients to use an MDI properly or using a spacer is essential to assure adequate dosage. It is dosed as 2 puffs q i d, plus prn, not to exceed 24 puffs/day. If higher doses of a beta-agonist are needed to control symptoms, the patients should be seen by their physicians.

Theophylline has a long history of use in patients with COPD and is used by many clinicians as a step-three drug. Although the precise role of theophylline in COPD management is still a matter of debate, it appears to benefit a subgroup of patients with severe stable disease. Theophylline's disadvantages are its low therapeutic to toxic ratio and its side effect profile. Therapy should be continued only if significant improvement occurs in symptoms or airflow obstruction. The major benefits of theophylline occur at serum levels of 10 to 15 $\mu\text{g/mL}$, so maintaining serum levels in this range maximizes benefits and avoids side effects. This is generally achieved as dosages of 400 to 800 mg/day. After starting a patient on theophylline, checking serum levels to assure a therapeutic and safe dosage is prudent. Subsequent levels should be rechecked if side effects develop, new drugs are prescribed, or if changes occur in the patient's condition.

Another second line agent is corticosteroid. These agents should be reserved for patients with inadequate symptom control using beta-agonists, ipratropium, and theophylline. A predictor of steroid response is a significant bronchodilator response during spirometry. If steroids are started, spirometry should be obtained before and after a 2-week trial of 40 mg/day dose of oral prednisone. A significant response is a 15% or greater improvement in FEV1. For patients with significant improvement, the steroid dose should be reduced to the lowest level that maintains the improvement. Steroids should be discontinued in patients without objective evidence of response, unless they are severely disabled and report significant subjective improvement. Since chronic oral steroids are associated with a multitude of side effects, some clinicians add inhaled steroids in the hope that they can reduce the oral steroid dose. Inhaled steroids, unfortunately, appear to have little value in COPD patients (6).

Acute Exacerbations

Three cardinal symptoms—increased sputum volume, increased sputum purulence, and increased dyspnea—mark an acute exacerbation of COPD. Exacerbations are often attributed to infection and tend to occur more frequently in the winter. Patients with exacerbations of COPD are usually treated with antibiotics, although the evidence to support this practice is mixed. Antibiotic therapy should target the most likely pathogens: *H. influenzae*, *M. catarrhalis*, and *S. pneumoniae*. The most commonly used agents are

trimethoprim-sulfamethoxazole, tetracyclines, amoxicillin, and amoxicillin/clavulanate. Extended spectrum macrolides, second-generation cephalosporins, and fluoroquinolones have also been used but are more expensive. The usual course for acute bronchitis is 7 to 14 days; clinical improvement should be evident in 2 to 4 days.

Oxygen Therapy. Oxygen is an important therapy because it is a potent pulmonary arterial vasodilator in hypoxic patients. For patients with chronic hypoxemia supplemental oxygen significantly decreases morbidity and mortality (7). Indications for long-term supplemental O_2 are:

$PaO_2 < 55$ mm Hg or $SaO_2 < 88\%$; $PaO_2 = 56$ – 59 mm Hg or $SaO_2 < 89\%$ and evidence of cor pulmonale; documented oxygen desaturation ($PaO_2 < 55$ mm Hg or $SaO_2 < 88\%$) during exercise or sleep.

Administration by nasal cannula is the most commonly used home delivery system. Oxygen flow is adjusted to the lowest flow needed to raise the PO_2 above 60 mm Hg or the oxygen saturation between 90% to 94%. Many clinicians increase the baseline flow by one liter per minute during exercise or sleep (8).

Respiratory Failure. During an acute exacerbation of COPD, respiratory failure may develop despite intensive therapy. Mechanical ventilation should be considered in patients with progressive acidosis and a rising PCO_2 , particularly in patients with clouded consciousness and respiratory muscle fatigue. Other indications include inability to maintain adequate oxygenation (particularly in association with hemodynamic compromise), rising respiratory rate, inability to clear secretions, and apnea.

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Respiratory Diseases in Infants and Children

Mitchell S. King

Respiratory diseases are among the most common illnesses presenting to primary-care physicians caring for children. This chapter will discuss some of the significant respiratory problems that primary-care physician will encounter.

BRONCHIOLITIS

Bronchiolitis is an episode of wheezing associated with an upper respiratory viral infection in infancy, occurring during the winter months, especially from December to March. Bronchiolitis occurs in children during the first 2 years of life, with most clinically significant disease occurring in children less than 1 year of age, and more severe disease occurring at less than 3 months of age.

Respiratory syncytial virus (RSV) accounts for 50% or more of cases, with the remaining cases caused by parainfluenza, adenoviruses, influenza, mycoplasma, or other viruses.

The virus causing bronchiolitis is usually acquired from an adult or child with an upper respiratory infection. The incubation period is about 5 days. A prodrome of an upper respiratory infection occurs for a few to several days with or without fever, with subsequent development of dyspnea, cough, and wheezing. Patients may have decreased appetite because of the difficulty feeding at higher respiratory rates.

Physical examination will reveal tachypnea, with respiratory rates of up to 60 to 80 breaths per minute, along with auscultatory findings of widespread rales, prolonged expiration, and wheezing.

Cyanosis, nasal flaring, use of accessory muscles of respiration, and retractions may be present.

Chest x-ray (CXR) findings are consistent with air trapping and show hyperinflation along with atelectasis. Oxygen saturation and PCO_2 are often decreased, although in more severe cases CO_2 retention may occur. White blood counts are often normal. Nasopharyngeal washings for enzyme limited immunosorbent assay (ELISA)/immunofluorescence testing for RSV are often positive. Other cultures or serologic testing are less useful clinically.

Management depends upon disease severity. Important factors in deciding for or against which children require hospitalization include:

1. Appearance of the child
2. Respiratory rate >60
3. Need for intravenous hydration
4. Hypoxia
5. CO_2 retention
6. Reliability of parents and follow-up care
7. Presence of underlying lung or cardiac disease

Humidified oxygen is administered to maintain an O_2 saturation $>92\%$, and in those children requiring hydration or supplementation of oral intake, intravenous fluids are administered. Beta adrenergic agonists can be tried, and if a good response is noted, can be continued in hospital or as outpatient therapy. No role currently exists for steroids, antibiotics, or theophylline in this disease. Some evidence has been reported that racemic epinephrine can be of benefit to these children, though further study of its role is necessary (1). The critical phase of this illness generally lasts 48 to 72 hours, during which hospitalization or close outpatient follow-up is needed.

Ribavirin (6 gm in 300 cc preservative-free water by aerosol continuously for 12 to 18 hours daily for 3 to 7 days) is an antiviral agent specific for RSV that is indicated for impending respiratory failure and high-risk groups, such as those with history of cyanotic heart disease, bronchopulmonary dysplasia (BPD), cystic fibrosis or other chronic lung conditions, immunodeficiency states, increasing CO_2 , $\text{PO}_2 < 65$, and age < 6 weeks (2). Ribavirin may cause ventilator malfunction, and should only be used with special filters in these patients. In addition, respiratory syncytial

—intravenous immunoglobulin (RSV-IVIG) has recently been licensed for treatment of infants with RSV infection who are less than 24 months of age and who have bronchopulmonary dysplasia, or less than 1 year of age and who have a history of premature birth. In these infants, it shortens the duration of hospitalization and lessens the severity of illness (3).

Prognosis is good, with a mortality rate of $<1\%$, and full recovery in the remainder. Up to 50% of affected children will have recurrent episodes of wheezing until age 2 to 3, with some of these children developing classic asthma.

PNEUMONIA

Respiratory infections are the most common infections in children, with pneumonia accounting for 10% to 15% of respiratory infections, resulting in significant morbidity and mortality. Impaired host defenses, most commonly preceding viral upper respiratory infection, predispose a patient to develop pneumonia. Other predisposing factors are immunodeficiencies, underlying lung or anatomic defects, and iatrogenic causes, such as intubation, tube feedings, and anesthesia. Because of the association with viral infections, pneumonia is more common during the winter months.

Clinical presentation and etiologic agents will vary with age, with different patterns being present in neonates (0 to 3 months), infants and children ages 3 months to 5 years, and children older than 5 years of age (Table 12.1). Hypoxemia correlates with severity of illness and can be present with any of the etiologic agents listed.

Management begins with an evaluation of the patient to determine disease severity and etiologic agent. This will include determining oxygen status, particularly in children who are dyspneic or appear toxic. Chest x-ray should be included, as well as a CBC and blood cultures. Sputum cultures and gram stain are difficult to obtain in children. Nasopharyngeal washings for viral analysis can be obtained. Urine for latex agglutination can also be helpful for detecting pneumococcal and *H. influenza* pneumonia. The CBC typically will show a neutrophilia and left shift for bacterial pneumonias, a lymphocytosis for viral pneumonias, and an increased eosinophil count with chlamydia. Blood for serologic testing can be useful for detecting mycoplasma and chlamydial pneumonias (4).

Table 12.1.
Pediatric pneumonias.

Age	Common Etiologic agents	Classic Presentation	Therapy	Comments
0–3 months	Group B strep Gram-negative organisms	Nonspecific findings, toxic appearance or respiratory distress shortly after birth. CXR with lobar infiltrate.	<ul style="list-style-type: none">• Ampicillin 100–200 mg/kg/24 hr q 8–12 hr, plus gentamicin 2.5 mg/kg/dose q 8–24 hr (dependent upon age) or cefotaxime 100–150 mg/ kg/24 hr divided q 8–12 hr.	Other less common organisms: Groups A and G strep, staph, myco- plasma, ureaplasma, pneumocystis, CMV.
	Chlamydia trachomatis	At 4–12 weeks of age, staccato cough with or without lung findings. CXR with interstitial infiltrates.	<ul style="list-style-type: none">• Erythromycin 40 mg/kg/ 24 hr. divided q 6 hr.	
3 months–5 years	Viral	Signs of upper respiratory tract infection, with or without diffuse rales, wheezing, low-grade temp. CXR with interstitial infiltrate, atelectasis or localized infiltrate.	Supportive	Viral etiologies most common.
	Atypical bacteria <ul style="list-style-type: none">• Chlamydia• pneumoniae• Mycoplasma		<ul style="list-style-type: none">• Erythromycin as above	Alternate therapies could include clarithromycin and amoxicillin/clavulanic acid for atypical or bacterial pneumonias.
	Bacterial <ul style="list-style-type: none">• pneumococci	More ill appearing, fever, cough, dyspnea, with	<ul style="list-style-type: none">• Amoxicillin 40 mg/kg/24 hr divided q 8 hr.	

Table 12.1 (continued).
Pediatric pneumonias.

Age	Common Etiologic agents	Classic Presentation	Therapy	Comments
	<ul style="list-style-type: none"> • H. influenza 	more localized lung findings. CXR with lobar infiltrate.	<ul style="list-style-type: none"> • Ceftriaxone 50–100 mg/kg/day 	
5 years and older	Bacterial: <ul style="list-style-type: none"> • pneumococci • Mycoplasma • Chlamydia pneumoniae • H. influenzae 	Bacterial same as above; atypical bacteria usually with nontoxic appearance	<ul style="list-style-type: none"> • Erythromycin as above • Clarithromycin 7.5 mg/kg/bid • Amoxicillin ± clavulanic acid as above • Ceftriaxone 50–100 mg/kg/24 hr. 	Bacterial etiologies, particularly atypical bacteria much more common. Other less common organisms: Legionella, staph, Strep pyogenes.
	Viral		Supportive	

Therapy will include intravenous hydration and oxygen if needed, and empiric antibiotics to cover likely pathogens according to the age of the child (Table 12.1). For those children requiring hospitalization, intravenous antibiotics should be continued until the child is afebrile for 48 to 72 hours and oral antibiotics continued for 10 to 14 days, except for *Legionella* and neonatal chlamydial disease, which require 14 to 21 days of therapy.

The prognosis for full recovery is excellent. The cough with atypical pneumonias can sometimes last 3 to 4 weeks. Chest x-ray findings should revert to normal after 4 to 6 weeks. Children with recurrent or persistent pneumonias require further evaluation and consideration for other infections (e.g., tuberculosis) and diseases leading to or presenting as pneumonia, such as tracheoesophageal fistula, gastroesophageal reflux, asthma, immunodeficiencies, neuromuscular disorders, cystic fibrosis, foreign bodies, and other anatomic/host defects predisposing to recurrent pneumonia.

STRIDOR IN CHILDREN

Stridor is a physical and/or historical finding wherein a harsh, high-pitched inspiratory sound indicates narrowing of the larger airways, most commonly resulting from croup, epiglottitis, or foreign body aspiration. Variable amount of respiratory distress occurs, and management of these causes differs.

Laryngotracheobronchitis (Croup)

Croup, which accounts for almost 90% of cases of stridor, generally results from a viral respiratory infection in children 6 months to 3 years of age. The etiologic agents are most commonly parainfluenza viruses 1, 2, or 3, but also may include influenza, adenovirus, RSV, or mycoplasma. These viruses cause inflammation and narrowing of the trachea and subglottic regions leading to obstruction of air entry. Croup generally occurs during the winter months.

The typical presentation is that of an upper respiratory infection with a low-grade fever then developing into a barking cough after 2 to 3 days, stridor, and in more severe cases, respiratory distress and cyanosis. Retractions are generally present, and the child may be agitated, or if in severe distress, obtunded.

Croup is a clinical diagnosis, and laboratory studies are generally not helpful. Pulse oximetry and blood gases can be normal. Neck x-rays may show the classic "steeple sign," indicating airway

narrowing in the subglottic region. Chest x-ray may reveal pulmonary infiltrates. Laboratory and x-ray testing, however, are generally not helpful and should be minimized to avoid agitating the child, while treatment is begun.

Less than 10% of affected children require hospitalization. Supportive measures include intravenous fluids, for children in significant distress or with signs of dehydration, oxygen mist tent (with care not to overcool the child), and close monitoring. Racemic epinephrine 0.5 cc of 2.25% solution in 3 cc normal saline as well as dexamethasone 0.6 mg/kg can help with airway edema. Racemic epinephrine can be repeated after 15 to 30 minutes. Caution should be exercised in use of this medication, however, as rebound edema and systemic side effects may occur after apparent successful use of epinephrine. Children requiring more than one epinephrine treatment should be hospitalized for observation. Dexamethasone is administered as a one-time dose of 0.6 mg/kg IM or intravenously. Repeated doses have shown no added benefit. Dexamethasone can be administered as outpatient therapy in patients with less severe disease and requiring no more than one epinephrine treatment (5).

Patients in severe distress requiring repeated epinephrine (hourly or more for several treatments) may require intubation, which should be done by a skilled individual under controlled circumstances with the child sedated. Extubation can be achieved generally within 72 hours or when a leak occurs around the endotracheal tube. Prior to extubation, three doses of dexamethasone should be administered to lessen edema and inflammation resulting from combined effects of intubation and the disease process.

Spasmodic Croup

Spasmodic croup is a variant of croup related to atopic disease and is generally less severe, presenting with a normal examination except for stridor or minor respiratory distress. The classic onset is a 1- to 3-year-old child with onset of stridor at night, not necessarily associated with an upper respiratory infection. A family or personal history of spasmodic or atopic disease is often present. No laboratory or x-ray studies are helpful, and these children respond to steamy or cool mist or to exposure to cool air. The response to racemic epinephrine is variable, and steroids are not indicated. Repeated episodes may warrant investigation for structural or anatomic anomalies as the cause.

Prognosis is good, though some association has been noted with later development of reactive airways disease. Recurrences in children older than 5 years of age are uncommon.

Epiglottitis

Epiglottitis is a life-threatening bacterial infection of the epiglottis and surrounding tissues leading to obstructive respiratory disease. More than three-fourths of the disease is caused by *Haemophilus influenza* type B, but may also be caused by Group A streptococcus, pneumococcus, or staphylococci. The incidence of this disease has greatly decreased in children since introduction of the *Haemophilus* vaccine. No seasonality or gender predilection occurs for epiglottitis.

Epiglottitis occurs in children ages 2 to 6 years old, with patients appearing acutely ill, often with fever in excess of 39.5°C. The onset is abrupt, with progression of disease over the course of hours. The child may complain of sore throat, difficulty swallowing, and have stridor, drooling, agitation, and muffled speech. The child may refuse to lie down, and cough is absent.

Urgent management should not be delayed for laboratory studies or x-ray unless the patient appears stable and the diagnosis is questionable. The sick child with apparent epiglottitis should be taken to the operating room in a controlled setting for performance of laryngoscopy with visualization and subsequent intubation. Then laboratory studies can be drawn, intravenous access obtained, and antibiotics started. A CBC, blood cultures and urine for counter-immunoelectrophoresis (CIE) can provide evidence of the infecting organism. As many as 90% of patients will be bacteremic. The classic lateral soft tissue neck x-ray findings include the thumbprint-like projection of the epiglottitis.

The goal of therapy is to maintain a patent airway while the disease is being treated. Controlled intubation should be performed along with intravenous fluids and antibiotics, either ceftriaxone (100 mg/kg/24 hr) or ampicillin (200 mg/kg/24 hr) plus chloramphenicol (100 mg/kg/24 hr), both of which are continued for 24 to 72 hours. Extubation can be considered after a leak develops around the tube and visualization of the decrease in inflammation of the epiglottitis is performed. Antibiotics are continued for 7 days, with oral antibiotics started after extubation.

The patient and all family members, if there are children less than age 4, should be given prophylaxis with rifampin. The rec-

recommended dose for rifampin prophylaxis is 20 mg/kg/day with a maximum 600 mg/day for children older than 1 month, and 10 mg/kg/day for infants less than 1 month. The prognosis for full recovery is good.

Foreign Body Aspiration

Foreign bodies (FB) must always be considered in the differential diagnosis of stridor, even with no history of FB ingestion/aspiration. The most common ages of occurrence for FB aspiration are 3 months to 6 years, with 69% occurring in children less than 6 years of age (6). The most common objects responsible are toys (balloons and objects with small parts), food and coins. These objects may or may not obstruct the airway and can act as a ball-valve.

Children with FB aspiration may have few or no symptoms or may present acutely with respiratory distress. The classic triad of symptoms is wheezing, cough, and decreased breath sounds. Other symptoms may include cough, dysphagia, stridor, pain, and dyspnea. Laboratory evaluation is not helpful. Chest x-ray may be normal or show hyperinflation (owing to the ball-valve effect), atelectasis, infiltrate, or visualization of the FB. If there is high suspicion and the chest x-ray is normal, expiratory or lateral decubitus films should be obtained, as they will reveal more subtle degrees of hyperinflation. Diagnosis is then confirmed and removal of the object performed by bronchoscopy. Acute episodes of FB aspiration presenting with severe respiratory distress would be managed according to Basic/Advanced Cardiac Life Support (BLS/ACLS) guidelines or with emergent bronchoscopy, if available. Antibiotics are not necessary unless a secondary pneumonia develops. Prognosis is good and full recovery should be expected.

ASTHMA

Asthma is recurrent, reversible airway obstruction and inflammation triggered by hyperresponsiveness to infectious or environmental factors. Locally acting inflammatory mediators stimulate edema, increased mucus production, and smooth muscle contraction. The initial triggers can be airway irritants (e.g., smoke), bacterial or viral infections, or true allergens. In children under age 5, viral infections are the most common trigger, with repeated RSV infections being linked to subsequent asthma.

After age 5, particularly in late childhood and adolescence, allergens are commonly the triggers. Crowded living conditions and airborne irritants in urban areas, as well as modernization of housing with conducted air heating/cooling and carpeting are thought to contribute to recent increases in incidence of asthma and asthma severity. Heredity plays a significant role in tendency toward atopy and asthma, with marked increases in incidence with a positive parental history of asthma.

Patients with asthma have recurrent episodes of wheezing, cough, and decreased exercise tolerance, associated with viral infections, atopic dermatitis, and/or allergic rhinitis. Physical signs of asthma may include wheezing, prolonged expiration, increased AP chest diameter, hyperresonance to percussion, and decreased breath sounds. Chest x-ray may show hyperinflation and/or areas of atelectasis. Testing for obstructive airway disease to confirm the clinical suspicion of asthma should include pulmonary function tests (PFTs) in children old enough to cooperate (age ≥ 5 to 6). Use of bronchodilators with PFTs increases the sensitivity of the testing by showing reversibility, as do provocative tests such as exercise testing, wherein a worsening forced expiratory volume at one second (FEV1) after exercise suggests the diagnosis. Peak flow can be substituted when PFTs are unavailable. The predicted peak flow varies with height of the child. Values 80% or less than predicted suggest obstruction and less than 50% indicate severe disease. Arterial blood gases should be obtained with acute episodes and would be expected to show decreased PO_2 and PCO_2 , with normal or increasing PCO_2 indicating worsening clinical status.

Treatment of asthma can be broken down into acute and chronic therapies, with differing intensities of therapy for differing levels of disease severity (Table 12.2). Disease severity is determined by peak flow, arterial blood gases (ABGs), and appearance of the child. Auscultatory findings can be misleading, as a child with severe asthma can have decreased air movement and thus quiet lungs. In children too young to perform peak flow, appearance (i.e., retractions/accessory muscle use) and ABGs should be assessed. For children with milder symptoms, pulse oximetry can be helpful along with peak flow and clinical appearance. Hospitalization is indicated for those children who, despite treatment, have a pulse oximetry less than 95% and/or peak flow less than 70%.

Table 12.2:
Asthma therapy in children.

	β -agonist	Anti-inflammatory	Other	Comments
Acute mild-mod. (PF 40–70 + %)	Albuterol 0.5cc in 3cc NS q 3–4 hr	Corticosteroids: prednisone 1–2 mg/kg/day methylprednisolone 1–2 mg/kg/q 6 hr. i.v.		Mild episodes may be managed with oral or aerosol/MDI β -agonist alone.
severe (PF < 40%)	Albuterol as above q 20–60 minutes	Methylprednisolone dosed as above	Epinephrine 0.01 mg/kg max. 0.3 mg SQ Aminophylline • 6 mg/kg initial load • 0.8–1.0 mg/kg/hr maintenance, for children older than 12 months, with subsequent dose adjusted for serum level 8–15 micrograms/ml	<ul style="list-style-type: none"> • Epinephrine used in patients in very severe distress, or unable to generate a peak flow. • Aminophylline used less commonly, and as add-on therapy for refractory cases. • 1 mg/kg load will increase serum level by 2 microgram/ml. • β-agonist drips also can be used for severe refractory cases.

Table 12.2 (continued).
Asthma therapy in children.

	B-agonist	Anti-inflammatory	Other	Comments
Chronic	Albuterol MDI 2 puffs q 4–6 prn	Cromolyn sodium: • MDI 2 puffs q 6 hr	Theophylline 18–22 mg/kg/day divided q 6 hr for children older than 12 months	Cromolyn or nedocromil are used as first-line anti-inflammatory agents in children for chronic treatment.
	Oral susp. 0.1 mg/kg/dose q 6–8hr	• Nebulizer 1 amp. q 6 hr		
		• Nedocromil MDI 2 puffs qid		Theophylline useful as add on for difficult to manage patients, or for nocturnal symptoms.
		• Beclomethasone or triamcinolone MDI 2 puffs tid-qid		

Chronic therapy involves utilization of beta adrenergic agonists for acute symptoms and anti-inflammatory medications for maintenance/prevention of symptoms. Anti-inflammatory medications should be utilized when beta-agonists are required more than three times per week, or peak flow remains $<80\%$ predicted or by history, or the patient's personal best. For administering chronic therapies, some nebulizer treatments can be given, or metered dose inhalers (MDI) can be provided along with proper instructions for MDI use and a spacer device. Other medications used for chronic, severe asthma include anticholinergic medications and methotrexate, and less commonly, systemic corticosteroids.

Peak flow measurement should be part of the chronic treatment regimen to monitor effectiveness of therapy and to assess for signs of worsening disease. More than 20% variance in twice per day peak flows or values less than 80% of predicted/personal best indicate need for adjusting therapy. Vaccines for influenza and pneumococcus should be given to patients with asthma.

The home environment of the child with asthma should be assessed, particularly those in whom allergy seems to be a significant factor. Presence of smokers, pets, carpeting, stuffed animals, excess humidity as well as other irritants/allergens may need to be addressed to control the asthmatic symptoms. Allergy testing through serum or dermal testing may be indicated to diagnose the allergy or convince the parents of the need to change the environment.

Prognosis varies, with up to half of patients having their asthma remit with time. The chances of this diminish with increasing age if the patient has persisting symptoms of asthma, hypoxia, or abnormal PFTs. Consultation with a pulmonologist or allergist should be sought for severe or resistant disease, atypical disease, allergy evaluation, or when the diagnosis is in question. Other causes of wheezing (e.g., sinusitis, gastroesophageal reflux) should always be considered in the evaluation of the child suspected of having asthma.

CYSTIC FIBROSIS

Cystic fibrosis is a genetic disease transmitted as an autosomal recessive trait, with 5% of Caucasians carrying the gene. It is one of the most common chronic respiratory diseases of children. Cystic fibrosis has varied presentations, ranging from infertility to severe respiratory disease with or without pancreatic insufficiency,

with several variations in degree of aggressiveness of the disease. This occurs because approximately one-third of affected children acquire the disease as a result of mutations, and these children tend to be less severely affected and have variant forms of the disease. The genetic defect causes hyperviscous secretions in the respiratory, gastrointestinal, and reproductive tracts. In the respiratory tract this leads to poor mucus clearance, propensity to infections, and airway destruction. In the gastrointestinal tract this commonly leads to bowel obstruction or pancreatic fibrosis and insufficiency with resultant malabsorption, failure to thrive, and increased risk for developing diabetes mellitus. In the reproductive tract this leads to infertility.

Children with recurrent respiratory disease (>two pneumonias in 12 months, sinusitis, reactive airways), failure to thrive, meconium ileus, hyponatremic dehydration (because of increased sodium loss in sweat), rectal prolapse, or positive family history should be considered for evaluation for cystic fibrosis. Diagnosis requires a history of recurrent obstructive pulmonary disease, along with pancreatic insufficiency or positive family history, and positive pilocarpine iontophoresis sweat test value (>60 mEq chloride/L) (7). False positives and negatives can occur due to poor technique or concomitant disease, and if required, genetic testing can be performed.

Therapy focuses on treating pulmonary infections, postural drainage to aid pulmonary mucus clearance, and maintaining nutritional status by providing the increased number of calories required in these patients along with fat-soluble vitamins and pancreatic enzymes. Additional therapies recently being utilized include aerosol treatments using DNAase or amiloride to improve respiratory mucus clearance, and oral ibuprofen or prednisone to lessen the inflammatory response/damage to the lungs (8, 9). These patients die as a result of pulmonary complications or, less commonly, hepatic failure. With improvements in therapy, many are now living to ages of 25 to 30 years or more.

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Problems of the Gastrointestinal System

Chapter 13

Medical Problems of the Gastrointestinal Tract

Joseph J. Nidiry

This chapter will discuss the diseases of the gastrointestinal tract with special emphasis on those commonly encountered in primary-care practices. Medical problems of the GI tract account for 25% of visits to physicians' offices.

DYSPHAGIA

Dysphagia or difficulty swallowing is the sensation of impaired movement of a bolus between the pharynx and the stomach. Dysphagia could be oropharyngeal or esophageal. Oropharyngeal dysphagia (transfer dysphagia) is characterized by a bolus being

caught up in the throat or neck region in association with coughing or nasopharyngeal regurgitation. Diseases affecting the muscles of mastication and deglutition (CVA, myasthenia) are responsible, and a contrast study using barium will establish diagnosis.

Esophageal dysphagia is characterized by a bolus "hung up" substernally, and is caused by diseases involving the lumen or smooth muscle of the esophagus. Dysphagia for solids indicates presence of partial, fixed, lumen obliterating lesions. Rapidly progressive dysphagia associated with weight loss suggests carcinoma of the esophagus. Dysphagia that is slowly progressive over months or years suggests benign stricture of the esophagus. Intermittent dysphagia for solids or acute complete obstruction of the esophagus suggests an esophageal ring or web (Schatzki's ring). Schatzki's rings occurring in 10% to 15% of upper GI series, are symptomatic only when the lumen is less than 13 mms. Dysphagia for both solids and liquids suggests an esophageal motor disorder, such as achalasia. The esophagus is aperistolic, with impaired relaxation of the lower esophageal sphincter. Esophageal foreign body is manifested by inability to swallow even saliva, without regurgitation.

Odynophagia is pain on swallowing, characteristically a severe, sharp substernal pain and is suggestive of ulcerative esophagitis, as occurs with radiation, infection and, lodged pills. Candida is most common cause of infectious esophagitis. Pill-induced esophageal ulcerations are being reported more frequently, especially in the elderly population (Doxycycline, KCl, NSAID).

All patients with dysphagia should have endoscopy. Barium swallow and motility studies are indicated if a motor disorder is suspected. Treatment depends on the underlying cause. Dysphagic patients with oral thrush (e.g., due to immunodeficiency) are treated with antifungal agents. Pneumatic dilation and calcium channel blockers will help in achalasia. Viscous xylocaine and withdrawal of medication will relieve pill-induced esophagitis.

Reflux Esophagitis

Reflux esophagitis is a chronic disorder that usually begins in adults over the age of 40 and is typically characterized by recurrent heartburn and occasional regurgitation. Gastroesophageal reflux disease (GERD) is also associated with manifestations (dental caries, pharyngitis, dyspaurunia). Peptic stricture (4% to 20%) and Barrett's esophagus (10% to 15%) are the most com-

non serious complications. Barrett's esophagus increases the risk for adenocarcinoma of the esophagus.

Medical therapy for reflux consists of lifestyle modification and drug therapy. Cessation of smoking, avoidance of acid stimulation, and weight reduction, along with elevation of the head of the bed and maintaining an upright position 2 to 3 hours postprandially are helpful. Liquid antacids are helpful for the rapid relief of symptoms but are not beneficial for long-term therapy. H₂ blockers are the mainstay in the treatment, dosages double those used for ulcer and for longer periods of treatment (months).

In patients who have predominantly nocturnal symptoms, prokinetic agents (metoclopramide and cesa-pride) are helpful. Metoclopramide, however, is associated with significant side effects.

Proton pump inhibitors are a new class of drugs that has been recently introduced for the treatment of esophagitis. By inhibiting the H⁺K⁺ ATPase system, these drugs are powerful, effective inhibitors of acid secretion. Omeprazole (Prilosec) 20 mg once or twice daily and lansoprazole (Prevacid 30 mg) once or twice are effective therapy. The combination of acid suppression and prokinetic agents has been found to be effective in refractory cases.

Availability of laparoscopic fundoplication has made surgical intervention more acceptable and is indicated in patients who are refractory to adequate medical therapy.

Carcinoma of the Esophagus

Squamous cell carcinoma of the esophagus is the most common neoplasm. It is 5 times more frequent in blacks and 3 to 4 times more in males than females. Predisposing factors are caustic esophageal injury, esophageal webs, longstanding use of alcohol or tobacco, longstanding achalasia without drainage, squamous carcinoma of the nasopharynx, and tylosis (an uncommon disorder characterized by hyperkeratosis of the esophagus, palms, and soles). Adenocarcinoma of the esophagus, in contrast, generally occurs in white males with longstanding history of reflux.

In patients presenting with dysphagia from carcinoma, weight loss is a universal finding. Endoscopy with biopsy and cytology will confirm the diagnosis. CT scan of the chest and endoscopic ultrasound will help in staging of the carcinoma.

Prognosis and 5-year survival still remain less than 5% despite the combination of chemotherapy followed by radiation and surgery. Palliative therapies include esophageal dilation, stent placement, and laser ablation of the tumor

Recurrent Noncardiac Chest Pain

Gastrointestinal causes, most commonly gallstones and reflux esophagitis, are thought to account for 40% of cases of recurrent chest pains. A causal relationship can be established only if appropriate treatment results in relief of symptoms. In patients who have persistent chest pains, ultrasound of the gallbladder, esophageal motility studies and 24-hour pH monitoring may be indicated. As these tests are neither specific nor sensitive enough, empiric trials with potent acid inhibitors such as omeprazole may be worthwhile. For patients with confirmed esophageal spasm by manometry, calcium channel blockers and bouginage may be helpful.

PROBLEMS OF THE STOMACH

Gastritis

Gastritis is classified as erosive, nonerosive, specific and nonspecific. Specific causes include bacterial, viral, and fungal infections, rarely Menetrier's disease (hypertrophic gastropathy), and eosinophilic gastroenteritis.

Erosive Gastritis

Erosive gastritis may be asymptomatic or may present with dyspeptic symptoms and gastrointestinal bleeding. The diagnosis is typically made by endoscopy, which shows erosions of the gastric mucosa and submucosal hemorrhage. The most common causes include topical injury from alcohol or NSAIDs and physiological stress due to severe medical and surgical illness. *Helicobacter pylori* may be a cause in children.

NSAIDs. Induced NSAIDs can cause diffuse subepithelial hemorrhage and small superficial erosions in the stomach in about a third of patients. The injury is most likely because of the inhibition of prostaglandin production by the gastric mucosa. Prostaglandins stimulate the production of mucus and bicarbonate by increasing mucosal blood flow and prolong the cell life of gastric mucosal lining.

Alcohol induces gastritis by injuring directly the gastric epithelium. The combination of NSAIDs and alcohol is associated with occurrence of mucosal damage in 100% of patients. Aspirin is the most ulcerogenic of all NSAIDs, and occurrence has been reported for dosages as low as 325 mg per day.

Stress-related mucosal disease occurs in many critically ill patients. Major risk factors include trauma, burns, hypotension, CNS injury, sepsis, mechanical ventilation, and multiorgan failure. Clinically evident bleeding from stress gastritis occurs in about 6% of untreated patients, while significant bleeding occurs in approximately 3%. The pathophysiology of stress-induced injury appears to be back diffusion of hydrogen ions from the gastric lumen caused by ischemic injury to the mucosa. The incidence of significant bleeding in ICU patients has decreased significantly due to improved supportive care and pharmacological prophylaxis, though a beneficial effect on mortality has not been demonstrated. Antacids, H₂ blockers (preferably by infusion), and sucralfate are of equal efficacy. Prophylaxis is not indicated in the absence of the above risk factors.

Helicobacter Pylori (*H. pylori*) Associated Gastritis

This is found in approximately 50% of people over the age of 60. Virtually all people in underdeveloped countries are infected by *H. pylori*, commonly acquired in childhood. In developed countries prevalence is low in early childhood but increases by approximately 1% per year of age. The bacterium, *H. pylori*, is a spiral flagellated Gram-negative rod that lives only in the mucus layer of gastric epithelial cells. The bacteria produce urease, which converts urea into ammonia, providing an alkaline medium around the bacteria that protects it from the effect of gastric HCL.

Diagnosis of *H. pylori* infection is best done by endoscopic biopsy of the antral mucosa. Urease activity in the biopsy specimen can be assessed by placing the specimen in a pH sensitive medium containing urea (CLO test). Ammonia produces a color change in the medium within 1 to 3 hours, which is presumptive evidence for *H. pylori*. This rapid assay has a sensitivity and specificity of 95%. Histologic examination of the biopsy specimen is the gold standard, but is more expensive. Cultures of mucosal specimens are less sensitive and are rarely performed. Noninvasive tests are the C13 and C14 urea breath tests, which are not yet readily available. This test also is 95% sensitive and specific, and will likely become the diagnostic test of choice.

H. pylori also causes an acute gastritis associated with transient clinical illness manifested by abdominal pain, nausea, and vomiting. The infection is associated with a transient decrease in HCL production. The proportion of patients who progress to chronic gastritis is not known. Chronic gastritis from *H. pylori* is present in approximately 30% of the U.S. population. The majority of patients are asymptomatic, with no indication for treatment. A four- to sixfold increased risk for development of adenocarcinoma of stomach with chronic gastritis owing to *H. pylori* has been reported. No recommendation has been made for treatment of *H. pylori* to prevent gastric carcinoma. Duodenal and gastric ulcer (see below) have been strongly associated with *H. pylori* infection. An association with non-Hodgkins lymphoma of the stomach and with low-grade B-Cell gastric (MALT) lymphoma have been reported.

The recent National Institutes of Health consensus conference on *H. pylori* recommends that the following group of individuals with *H. pylori* infection be treated.

1. Documented duodenal ulcer
2. Gastric ulcer with *H. pylori*

Atrophic Gastritis

Autoimmune gastritis causes achlorhydria and Vitamin B12 malabsorption owing to lack of intrinsic factor. The gastritis involves predominantly the fundus and the body of the stomach. Parietal cell antibodies are present in more than 90% of patients. High gastrin levels (>1000 pg) are present in these individuals, and these cause development of small carcinoid tumors in up to 5% of affected individuals. The risk of adenocarcinoma is slightly increased. Endoscopic biopsy reveals atrophy of glands, intestinal metaplasia, and minimal inflammation. Endoscopic surveillance is indicated in patients with gastric dysplasia or carcinoid tumors. No treatment is indicated other than for pernicious anemia when present.

Gastric Ulcer

Gastric ulcer occurs more frequently in the middle-aged and elderly. Three specific causes for peptic ulcer have been identified: *H. pylori* infection, NSAID use, and Zollinger-Ellison Syndrome. The characteristic clinical presentation is that of epigastric discomfort or pain. The typical rhythm of pain and relief with food

present in duodenal ulcer may be lacking, but relief with antacids is common. Patients with gastric ulcer may present with complications such as bleeding or perforation in up to one-third of patients without premonitory symptoms. Bleeding from gastric ulcer is more frequent than from duodenal ulcer, more massive when it occurs, and tends to recur more often.

NSAIDs induce serious gastrointestinal complications and are considered to be the most frequent cause for gastric ulcers. Approximately 2% to 3% of chronic NSAID users develop major gastrointestinal complication each year. Aspirin is the most ulcerogenic NSAIDs, and the incidence is dose-related. At equivalent doses, all NSAIDs are ulcerogenic except some of the newer NSAIDs such as Nebumetone and Etodolac, which are reputed to be less ulcerogenic. Chronic NSAID users have a 10% to 20% prevalence of gastric ulcers and 5% to 10% prevalence of duodenal ulcer. The relative risk for development of gastric ulcers is 40%. Approximately one-fourth of chronic NSAID users complain of dyspeptic symptoms, but half of them do not have erosions or ulcerations. Thirty percent to fifty percent of NSAID users with ulcers do not report any symptoms, and two-thirds of patients who develop ulcer complications such as bleeding or perforation deny having any previous dyspeptic symptoms. NSAID-induced complications are more likely with higher dosages, advanced age, history of previous ulcer disease, first 3 months of use, and concomitant corticosteroid use. *H. pylori* infection does not predispose to NSAID-induced gastric or duodenal ulceration. NSAID-induced platelet dysfunction may be another contributing factor in gastrointestinal bleeding.

The mechanism through which NSAID causes gastroduodenal ulceration seems to be damage to the mucosal layer. Both topical and systemic effects play a role, as parenteral NSAIDs such as ketorolac (Toradol) cause gastrointestinal damage.

H. pylori antibodies are found in approximately 40% of patients with gastric ulcer. While the role of *H. pylori* in recurrence of duodenal ulcer is clear and studies have demonstrated significant reduction in recurrence of Duodenal ulcer after eradication of *H. pylori*, the data regarding gastric ulcer are not clear. However, the recommendation is to eradicate *H. pylori* in patients with gastric ulcer if it is present.

Major complications of gastric ulcer are perforation and bleeding, both medico-surgical emergencies.

All patients with gastric ulcer should have endoscopy with biopsy and cytology at some point during the course, and gastric ulcer healing should be documented by x-ray or endoscopy because of the malignant potential.

Treatment for gastric ulcer will be discussed with that of duodenal ulcer.

Gastric Carcinoma

The majority of malignant neoplasms of the stomach arise from the mucous cells. Gastric cancer was the most common malignant disease in the United States until the 1940s. Since then, a significant decrease has been noted in the incidence of gastric cancer. In 1940, gastric cancer caused 22.5 deaths per 100,000, but currently the rate is only 7:100,000. Certain countries such as Japan, Chile, Costa Rica, Hungary, and Poland have extremely high rates for gastric cancer. Environmental factors such as poor refrigeration of food, which causes increased amount of nitrosamines, bacterial overgrowth in the stomach, and genetic factors have been implicated. Well-recognized risk factors for development of gastric cancer are intestinal metaplasia, pernicious anemia, and the postgastrectomy state. Gastric cancer is more common in males, in lower socioeconomic groups; more common in blacks than in whites, and the incidence increases with age, with few cancers occurring before age 40. Additional risk factors include family members with gastric carcinoma and blood group A.

The first symptoms, albeit after some progression, are usually early satiety, fullness in the epigastrium and weight loss. Most patients also will have anemia owing to chronic blood loss. Diagnosis is made by endoscopy with biopsy and cytology. Prognosis is poor, as most patients, by the time of diagnosis, will already have metastases. However, resectable lesions should be removed. Combination chemotherapy has demonstrated some improvement in survival.

DUODENAL ULCER

Approximately 10% of the population will be affected by the disorder during their lifetime, and 1% to 2% of the population have active disease at any one time. Based on data derived from hospitalizations for duodenal ulcer, it is suggested that a 40% to 50%

decrease has occurred in the incidence of duodenal ulcer during the past 2 decades. Hospitalization for complications, however, has not decreased significantly.

Increased acid output appears to be uniform in patients with duodenal ulcer. An increased incidence in males, in smokers and in users of NSAIDs has been established. The most current data, however, support a significant role for *H. pylori* infection in the etiology of duodenal ulcer. Up to 90% of patients with duodenal ulcer can be demonstrated to have *H. pylori* gastritis. Approximately 15% of infected individuals develop an ulcer over 12 to 25 years. The exact mechanism through which *H. pylori* causes ulcer is not known.

The typical symptoms of patients with duodenal ulcer are burning and gnawing epigastric pain occurring 3 to 4 hours after meals, frequently occurring at night or early morning, relieved by food and antacids. Pain may radiate through to the back in approximately one-fifth of patients. While the classical picture may be lacking, the vast majority of patients will have pain relieved by antacids.

In the preponderance of patients, the diagnosis can be suspected clinically and confirmed either by barium studies or endoscopy.

The major complications of duodenal ulcer are bleeding and perforation. Approximately 15% to 20% of patients with ulcer will experience gastrointestinal bleeding, and this is responsible for half of all hospital admissions for major upper gastrointestinal bleeding. The incidence of perforation is 7:100,000 to 10:100,000. Less common complications are pyloric obstruction and penetration of the ulcer to adjacent structures such as the pancreas. Duodenal ulcer is characterized by a tendency for recurrence, which 75% of patients will experience within 1 year.

Treatment of both gastric and duodenal ulcers has three objectives: relief of symptoms, healing of the ulcer, and prevention of recurrence. Antacids, H₂ blockers and sucralfate are effective in achieving the first two goals. The rate of healing of the ulcer depends on the degree of acid inhibition and duration of therapy.

H₂ receptor antagonists have been the mainstay in the therapy of ulcer. All of the four agents available are equally effective. Cimetidine, ranitidine, famotidine and nizatidine each will heal 90% of duodenal ulcers in 6 weeks and gastric ulcers in 8 to 12 weeks. For uncomplicated ulcers, a single bedtime dose may be sufficient.

Antacids are effective in the immediate relief of symptoms. Sucralfate, a mucosal protective agent, is also equally effective in healing peptic ulcers.

Proton-pump inhibitors (PPI) are a new class of potent acid inhibitors that has been recently approved for the treatment of peptic ulcers. Omeprazole and lansoprazole, two drugs in this category currently available, bind covalently to the proton-pump, inactivating it irreversibly. At a dose of 20 to 40 mg, omeprazole inhibits 95% to 100% of 24-hour acid secretion. Treatment with PPIs heals more than 90% of gastric ulcers *and* duodenal ulcers in 4 to 6 weeks. Up to 10% of peptic ulcers fail to heal after 8 to 12 weeks of H₂ blocker therapy. PPI therapy heals virtually all of these ulcers.

NSAID-induced ulcers heal rapidly with standard therapy when NSAIDs are discontinued. When NSAIDs cannot be discontinued, PPIs appears to be superior to H₂ blockers. Misoprostol, a prostaglandin analogue, is the only drug approved for prevention of NSAID-induced gastric and duodenal ulcers. No consensus has been reached as to which patients on NSAIDs should receive misoprostol prophylaxis.

The treatment and prevention of recurrence are major issues with peptic ulcer disease. Eradication of *H. pylori* has been shown to reduce recurrence by 95%. The recent NIH consensus conference recommended that all patients with peptic ulcer who have evidence of *H. pylori* receive antibiotic treatment for eradication of *H. pylori*. The recommended antibiotic regimen that is most successful (90%) is bismuth subsalicylate (Pepto Bismol) 2 tab 4 times a day, metronidazole 250 mg 4 times a day, and tetracycline 500 mg 4 times a day, for 14 days.

Dual therapy with PPI (omeprazole or lansoprazole) twice a day and a single antibiotic (amoxicillin 500 mg q.i.d., or clarithromycin 500 mg t.i.d.) appears to be equally effective.

Maintenance therapy with H₂ blockers is currently not recommended for prevention of recurrence of PUD. Courses of H₂ blockers, however, may be repeated in *H. pylori*-negative patients with recurrent ulcer disease.

FOOD POISONING

Food poisoning results from a direct nonimmunogenic action of ingested food or food additive that may be contained within the food or released by organisms contaminating food. Food sensi-

tivity reflects any immunologically mediated reaction to food or its constituents. Most food poisoning is manifested by nausea and vomiting with or without diarrhea.

Common Bacterial Food Poisoning

Bacterial food poisoning is due to one of several bacteria.

Salmonella species account for one-third of all nontyphoidal bacterial food poisoning. The incubation period is 6 to 48 hours, and the most common symptom is gastroenteritis. Symptoms typically last for a few days, and often no therapy is necessary. If antibacterial treatment is elected, trimethoprim-sulfamethaxazole is effective. This may be required when it occurs in an immunocompromised host, in the presence of a prosthetic device; or graft, valvular heart disease, hemolytic disorders, extremes of age, or evidence of systemic toxicity.

Staphyococcus aureus accounts for one-fourth of all cases, with an incubation of 3 to 6 hours, and symptoms of gastroenteritis resolve within 24 to 48 hours.

Clostridium perfringens accounts for 17% of nontyphoid cases, with an incubation of 8 to 24 hours and illness of short duration, usually less than 24 hours.

Vibrio parahemolyticus is frequently associated with seafood, produces watery diarrhea, and lasts for 24 hours.

Bacillus cereus has an incubation period of 9 to 18 hours, may cause either diarrheal disease or vomiting, and resolves in 3 days.

ACUTE DIARRHEAL DISEASE

Most acutely presenting cases of diarrhea have infectious causes and usually occur after the ingestion of food or water contaminated by bacteria or their toxins. Table 13.1 depicts etiology and clinical characteristics of common and uncommon causes of diarrhea. Most inflammatory diarrheas will have leukocytes in the stool, while noninflammatory diarrheas will not show stool leukocytes. Diagnosis is made by clinical suspicion and appropriate cultures.

INFLAMMATORY BOWEL DISEASE

The term refers to infectious and noninfectious inflammatory disorders of the large and small intestine. When specific etiologic agents are involved, usually the agent is mentioned (i.e., tuberculous colitis, amebic colitis) and specified in the designation.

Table 13.1.
Acute diarrhea syndromes: exposure and clinical characteristics.

Etiology	Exposure	Clinical Characteristics
Inflammatory Diarrhea		
Nontyphoidal salmonella shigella	Poultry, beef, pork, eggs, travel Exposure to children, travel, male homosexuality, institutionalization	+ Chills + watery stools + dysentery in 10% + Watery stools + dysentery in 30% + Hemolytic uremic syndrome
Campylobacter	Milk, chicken, animals	± 2d prodrome (fever, myalgia, headache) then + watery diarrhea + abdominal pain + Occasional dysentery
Yersinia Vibrio parahaemolyticus	Dairy, pork, beef Seafood in summer months	Simulate appendicitis + Fever in 25% + explosive diarrhea + nausea + vomiting + abdominal pain
Enterohemorrhagic <i>Escherichia coli</i>	Meat, dairy in restaurants, institutions	+ Severe abdominal pain fever + Bloody diarrhea + fecal leukocytes + Hemolytic uremic syndrome
Entamoeba histolytica	Travel, male homosexuality, daycare, institutionalization	From vague symptoms to fulminant colitis – Fecal leukocytes
Clostridium difficile	Antibiotic therapy	+ Fever, positive toxin assay + Lower abdominal pain + tenesmus
G.C. proctitis	Anal intercourse	+ Tenesmus + rectal pain

Acute diarrhea syndromes: exposure and clinical characteristics.

Etiology	Exposure	Clinical Characteristics
Radiation enteritis/colitis	History of radiation	+ Nausea and vomiting + fever + bleeding + Tenesmus (in radiation proctitis)
Staphylococcus aureus	Foods high in protein, salt, sugar	- Fever + Nausea + vomiting + abdominal pain
Bacillus cereus	Fried rice	
Norwalk virus	Salads, shellfish, water	+ Fever + headache + myalgia + Nausea + vomiting + abdominal pain
Clostridium perfringens	Meat, poultry	+ Severe abdominal pain - Fever - nausea - vomiting
Bacillus cereus-diarrheal syndrome	Improperly refrigerated foods	+ Abdominal pain - Fever - nausea - vomiting
Enterotoxigenic <i>Escherichia coli</i>	Travel	+ Fever + Abdominal pain
Cholera	Travel	- Fever + Severe watery diarrhea
Giardia	Travel, drinking from natural water sources, person to person	+ Fever + Bloating
Drugs	Recently started or increasing dose	- Fever
Fecal impaction	Bedridden, elderly	- Fever
Enteral feeding	Enteral feeding	+ Incontinence + stool in rectum - Fever - abdominal pain

The term *inflammatory bowel disease* (IBD) usually refers to idiopathic inflammatory bowel diseases, i.e., Crohn's disease and ulcerative colitis.

Crohn's Disease (Regional Enteritis)

Crohn's disease is characterized by a transmural inflammation with characteristic noncaseating granulomas, which can involve any part of the gastrointestinal tract. The inflammation tends to be focal and asymmetric. The focal and transmural inflammation accounts for the pattern of aphthous ulcerations, which may extend to form fissures, fistulas and perianal disease. The thickening of the affected loops with narrowing of the lumen account for the obstructive symptoms that many patients experience.

The incidence varies from 10:100,000 to 70:100,000, and Crohn's disease occurs most frequently in people of European descent, particularly Jews (6 times). It can affect any age, but peaks between 15 and 30 years. An increased familial incidence and an overall increase in the general population has been noted.

Diarrhea and abdominal pain are the most common presenting symptoms. The clinical picture, however, depends on the site as well as the extent of involvement of the gastrointestinal tract. Forty percent of patients have ileocolitis, 30% ileitis, and 20% colitis, and the remaining have involvement of any part of the gastrointestinal tract. Several extraintestinal manifestations occur in Crohn's disease, the most common being anal and perianal fissures and fistulae (22%), arthritis and arthralgias (18%), iritis and uveitis (4%), skin lesions (8%), liver disease (5%), and aphthous oral ulcers (1%).

Diagnosis of Crohn's disease is made by barium studies, endoscopy, and pathology. Infectious causes of diarrhea should be excluded.

Complications from Crohn's disease include intra-abdominal abscess, fistula between bowel and adjacent organs such as the vagina, bladder, or other loops of bowel. An increased incidence of cholelithiasis and nephrolithiasis occurs in patients with Crohn's disease. An increased incidence of cancer of small and large bowel has been reported.

Therapeutic options for Crohn's disease consist of antibiotics and anti-inflammatory drugs. Metronidazole has been found effective, especially in the treatment for perianal disease. Sulfasalazine and other aminosalicylates are effective in mild disease. In acute flare-ups corticosteroids are the drugs of choice.

Patients with Crohn's disease are often better treated in consultation of varying intensity with gastroenterologists, as the disease tends to have a chronic, protracted course. Surgery is indicated for complications such as obstruction or abscess or when disease is refractory to medical treatment. Surgery almost never is curative, as there is a high incidence of recurrence (75% in 5 years) after surgery.

Ulcerative Colitis

Ulcerative colitis is a diffuse continuous superficial inflammation that begins in the rectum and involves a variable extent of the proximal colon. The disease is limited to the colon and does not involve the small bowel. Pathologically, the colonic tissue reveals polymorphonuclear infiltration with destruction of the crypts (crypt abscess).

The clinical presentation depends on the extent and severity of inflammation. The symptoms usually evolve gradually, although occasionally an attack may be abrupt, following apparent infectious diarrhea. Patients with disease confined to the rectum have bloody diarrhea associated with urgency and tenesmus. More extensive involvement may be manifested with more severe diarrhea and bleeding. Symptoms tend to be more severe at night. One percent of patients may present with severe colitis (toxic megacolon) with fever, nausea, vomiting, abdominal distention, dehydration, anemia, and signs of impending peritonitis.

Diagnosis is made by sigmoidoscopic evidence of mucosal inflammation. Biopsy will reveal the described changes. Stool culture, examination for ova and parasites, and *C difficile* toxin assay should be performed on all patients to exclude other causes of colitis.

Treatment consists of corticosteroids to induce remission and sulfasalazine or its derivatives to maintain remission. Topical corticosteroids (steroid enema) or mesalamine (Rowasa enema) are effective in distal colitis and are associated with less systemic side effects.

Extraintestinal complications such as sclerosing cholangitis, central and peripheral arthropathies, ocular inflammation, erythema nodosum, and pyoderma gangrenosum occur to varying degrees in patients with Crohn's disease and ulcerative colitis. In the pediatric populations, IBD may present as fever of unknown etiology (FUO), arthritis, and retarded growth and sexual development. Pregnancy, oral contraceptives, and NSAIDs may aggravate symptoms.

Patients with longstanding ulcerative colitis are at high risk for cancer of the colon. The duration and extent of colitis, and possibly concurrent liver disease are cofactors that increase the risk of carcinoma. It is recommended that patients with ulcerative colitis for more than 10 years (independent of disease severity or therapy) undergo surveillance colonoscopy with biopsy on a yearly basis. Confirmed dysplasia by biopsy is an indication for colectomy.

Diverticulosis and Diverticulitis

Diverticular disease of the colon consists of herniation of the mucosa through defects in the muscular layer formed adjacent to the nutrient arteries. It occurs as a result of decreased stool volume inducing increased intraluminal pressure and muscle hypertrophy of the circular muscles. The prevalence is estimated to be present in 12% of the general population. It makes its appearance commonly before age 40 but is present in one-half of all autopsies of people over age 60.

Most diverticuli are asymptomatic, but they may be associated with three clinical syndromes: pain, bleeding, and inflammation. A high-fiber diet appears to decrease the incidence of diverticulitis. Treatment with high-fiber diet, increase fluid intake, and mild antispasmodics is often helpful for constipation and lower abdominal pains.

Diverticular bleeding is an uncommon complication of diverticulosis. Because of the frequency of diverticular disease, however, it is a common cause of severe lower GI bleeding, especially in the elderly.

Twenty percent of people with diverticulosis will develop diverticulitis at some time in their lifetime. It is caused by inflammation of the diverticulum due to irritation from inspissated stool. Diverticulitis most commonly presents as localized peridiverticular inflammation contained by pericolonic fat and mesentery. Usually only one diverticulum is involved and is confined to the sigmoid colon. Inflammation may extend in some cases, causing pericolonic abscess, fistula, rarely perforation and peritonitis. Classical symptoms are lower abdominal pain, fever, and change in bowel habits, either diarrhea or constipation. Urinary symptoms may occur if the inflammation extends to the bladder. Left lower quadrant tenderness with or without rebound and a palpable mass are characteristic findings.

Intestinal obstruction may be the presentation. CT scanning can define the extent of inflammation. Barium enema should be done only after symptoms have resolved.

Broad spectrum antibiotics to cover aerobic and anaerobic bacteria (third-generation cephalosporin, or aminoglycoside plus metronidazole) will result in improvement of symptoms in the majority of patients within 72 hours. Antibiotics should be continued for 7 to 10 days. Surgery is indicated for patients with evidence of peritonitis, free air, continued fever, obstruction, or urosepsis. Recurrent attack may be indication for resection.

Irritable Bowel Syndrome (IBS)

Irritable bowel syndrome is a localized manifestation of functional gastrointestinal disorder, characterized by abdominal pain and discomfort associated with altered defecation, without any structural changes that can be documented in the gastrointestinal tract. Alternating diarrhea and constipation and relatively young age of onset are characteristic features. Etiology remains unclear, and several hypotheses have been proposed. Relation to stress in precipitating symptoms has been well established. Lack of specific physical findings and laboratory abnormalities should point toward the diagnosis. Onset over age 40 is unusual, and in that age group, other organic pathology should be excluded before making the diagnosis.

Treatment is mostly symptomatic. Lactose and other carbohydrate intolerance may play a role in some individuals. Thus, dietary manipulation may improve symptoms in a significant number of patients. Increase of fiber in the diet has also been associated with clinical improvement. Anticholinergic and antispasmodic agents are helpful in many cases. Narcotic analgesics play no role in these patients.



Surgical Issues of the Gastrointestinal Tract

Cynthia M. Brown

THE ACUTE SURGICAL ABDOMEN

A gradual onset of periumbilical pain is typical of appendicitis, diverticulitis, or other inflammatory conditions arising from a midline derived organ below the ligament of Treitz. Colicky or cramping pain denotes supranormal contractions by a hollow organ, either irritated or obstructed. Midline crampy pain indicates obstruction of the bowel, cystic duct or common bile duct, and there may be periods without pain. Lateralizing colicky pain is nearly always due to ureteral obstruction. Progressively severe pain may indicate a condition that is worsening, such as ischemia of the bowel. Sudden "burning" pain suggests a perforated viscus. A dissecting aneurysm has a "tearing" pain. Pain may be referred to another area by somatic nerves. Pain of cholecystitis may be referred to the right sub-scapular area (Boas's sign), or bandlike around the right lower thorax; renal colic to the testicle, and subphrenic irritation to the ipsilateral shoulder. Anorexia, nausea and vomiting *follow* pain in appendicitis but *precede* pain in gastroenteritis. Changes in bowel habits from absence in obstruction to bloody diarrhea in various forms of colitis are useful information as well. Prior abdominal surgery predisposes a patient to adhesions that can cause intestinal obstruction. Food ingestion may be helpful, as food may alleviate the pain of peptic ulcer disease and aggravate the pain of cholecystitis or pancreatitis. In the female patient of childbearing years, a good obstetrical and gynecologic history must be taken for consideration of ec-

topic pregnancy, pelvic inflammatory disease (PID), and ovarian problems.

A patient with peritonitis will lie very still, and any motion will cause severe pain. A patient with a gallstone or kidney stone will move about trying to find a comfortable position. Nonabdominal causes of abdominal pain include pneumonia, diagnosable by history, examination, and ancillary studies.

One must look for jaundice, feculent breath, and signs of dehydration, and should inspect the abdomen for distention, visible peristalsis, dilated veins, spider angiomas, hernias, and surgical scars. A bluish discoloration of the umbilicus (Cullen's sign) may indicate hemoperitoneum (1). Ecchymosis on the abdomen or flanks (Grey-Turner's sign) is from massive hemorrhagic pancreatitis or strangulated bowel. Auscultated normal bowel sounds are high-pitched and occur every 5 to 10 seconds. If no sounds are heard in 2 minutes, they are considered to be absent, suggesting paralytic ileus. Rushes of high-pitched "tinkles," or borborygmi, are associated with increased peristalsis and seen in early intestinal obstruction.

Each quadrant is palpated deeply for localized masses and deep and rebound tenderness and for hernias. Percussion will help determine presence and focus of rebound tenderness, and the size of the liver and spleen, checking for fluid waves and shifting dullness of ascites. Tympany may suggest free air in the abdomen or air in the stomach or intestines. A rectal examination should always be performed when a patient has acute abdominal pain, checking for occult blood. Women should have pelvic examinations to rule out obstetric and gynecologic causes. Cervical cultures should be obtained. Males should have genital examinations when presenting with acute lower abdominal pain, as torsion of the testicle, a urologic emergency, presents with this and testicular pain.

A complete blood count (CBC) with differential and a urinalysis should be performed on all patients presenting with acute abdominal pain. Serum amylase, electrolytes, creatinine, and liver function tests should be ordered, depending on clinical circumstances. Urine pregnancy testing should be done on all women of reproductive age. Arterial blood gases may be indicated in severely ill patients. Table 14.1 contains some diagnostic features of common causes of the acute surgical abdomen. When the primary-care physician diagnoses an acute abdomen, surgical consultation should be requested upon admission.

Diagnostic features of the acute surgical abdomen.

Condition	Differential Diagnosis	Initial Symptoms	Physical Examination	Laboratory Findings	Imaging
Appendicitis	Gastroenteritis, PID, mesenteric adenitis, ruptured ovarian cyst, ectopic pregnancy	Periumbilical pain, nausea, anorexia, indigestion	T \leq 38°C (100.5 ° F), RLQ point-tenderness guarding, rebound, + psoas, + obturator sign	WBCs 15,000+, with left shift	Ultrasound (US) → edema of appendix, ileus on plane films
Cholecystitis	PUD, pancreatitis, high retrocecal appendicitis, perihepatitis	Abrupt onset of steady pain after meals in upper abdomen, fever, nausea, vomiting	Palpable gallbladder, tender RUQ, + Murphy's sign	WBCs 12,000–15,000 mild ↑ alkaline phosphatase bilirubin 2–4, ↑ amylase	Enlarged gallbladder on plain film; gallstones seen in 15%; US and HIDA scan show stones/sludge US shows gallstones in 95%
Cholelithiasis and chronic cholecystitis	Duodenal ulcer, hiatal hernia, pancreatitis and myocardial infarction	Steady RUQ pain, nausea & vomiting; pain may radiate to precordium, back and shoulder	Tender RUQ	Normal	
Perforated peptic ulcer	Acute pancreatitis, acute cholecystitis, intestinal obstruction	Sudden onset of upper abdominal pain several hours after a meal	“Board-like” rigid abdomen, bowel sounds—or ↓, tympany over liver	WBCs 12,000/μL+, mild ↑ serum amylase in paracentesis fluid	3-way abdomen → free air under the diaphragm

Table 14.1 (continued).
Diagnostic features of the acute surgical abdomen.

Condition	Differential Diagnosis	Initial Symptoms	Physical Examination	Laboratory Findings	Imaging
Bowel obstruction: duodenal	Gastritis, acute pancreatitis, acute cholecystitis	Vomiting bile, distended upper abdomen, pain	Normal to slightly ↑ T., epigastric tenderness, peristaltic rushes	Normal early → ↑ WBCs, ↑H/H, ↑ serum amylase, electrolyte abnormalities	Plain films→“double bubble” distended stomach and duodenum
Jejunum, ileum	Gastroenteritis, inflammatory bowel disease	Distended abdomen, colicky periumbilical pain, vomiting bile later, obstipation	Normal to slightly ↑ T., midabdominal tenderness, peristaltic rushes	Normal early → ↑ WBCs, ↑H/H, ↑ serum amylase, electrolyte abnormalities	Flat and upright plain films →ladderlike dilated loops of small bowel
Colon	Paralytic ileus, pseudo-obstruction (Ogilvie's syndrome), constipation	Deep crampy pain, abdominal distention, constipation, nausea, feculent vomiting (late)	Abdominal tenderness, distention, tympany, borborygmus, ± blood in rectum		Plain films → “picture frame”; BE confirms diagnosis and location; no barium PO!

Perforated Peptic Ulcer

Perforation is a potentially lethal complication of peptic ulcer disease, the most common cause of perforated viscus. It presents with sudden onset of severe upper abdominal pain and is rarely preceded by nausea and vomiting. The patient appears to be in severe distress, with the knees drawn up and breathing shallowly to decrease abdominal wall motion. The abdomen is involuntarily guarded with a rigid, boardlike feel. Tympany may be present over the liver, where it is usually dull from air between the liver and the abdominal wall. Bowel sounds are decreased or absent. In the early stages, the leukocyte count will be in the 12,000/ μ L range, rising to 20,000/ μ L or more in the next 12 to 24 hours. The serum amylase may rise (and a high level of amylase will be present in paracentesis fluid). Free air under the diaphragm can be seen on a free-way abdominal radiograph in 85% of cases. Free air can also be seen on a left lateral decubitus film. If no free air is seen, an upper GI series using barium (gastrograffin) should be performed if the clinical picture still suggests a perforated ulcer.

Treatment is begun by passing a nasogastric (NG) tube into the stomach to empty the contents and prevent further contamination of the abdomen. Intravenous antibiotics (e.g., cefazolin, cefotaxime) should be started. Laboratory studies should be obtained, fluid volume and electrolytes corrected prior to surgery. The perforation can be closed per laparoscopy or laparotomy. Perforation complicated by hemorrhage cannot be treated by simple closure and may need vagotomy plus gastroenterostomy, pyloroplasty, or gastrectomy. The presence of *H. pylori* should be ascertained, as it is present in 90% to 95% of duodenal ulcers and 70% to 90% of gastric ulcers (2). Its presence must be verified before treating to eradicate it. This can be done by serum IgG antibody study, breath test, or endoscopic biopsy. If positive, the patient is treated with an appropriate regimen to eradicate the ulcer and *H. pylori*. This serves to prevent recurrent perforation and gastric carcinoma (3). The mortality rate from perforated peptic ulcer is 15%, with one-third of these undiagnosed before surgery (4).

Cholecystitis and Cholelithiasis

The most common disease of the gallbladder is cholecystitis. Although most frequently associated with gallstones, only 30% of people with cholelithiasis go to surgery. The most common symp-

tom, biliary colic, is caused by obstruction of the cystic duct and may be felt in the right upper quadrant, epigastric, precordial, or left upper quadrant regions. Pain may radiate to the costal margin, circumferentially to the right upper back or scapula. Characteristics of the pain include abrupt onset, steady pain, sometimes occurring after meals and gradually subsiding over minutes to hours. Associated symptoms include nausea and vomiting. Physical examination reveals tenderness in the right upper quadrant and perhaps a palpable gallbladder. A positive Murphy's sign (5) is an inspiratory arrest on palpation of the gallbladder. The first diagnostic test should be ultrasonographic imaging of the gallbladder, which will demonstrate 95% of gallstones. If equivocal, an oral cholecystogram (OCG) may be obtained. About 2% of patients with gallstones will have negative ultrasounds and OCGs. Biliary colic may mimic the pain of duodenal ulcer, hiatal hernia, pancreatitis, myocardial infarction, and radicular pain in the T6–T10 distribution.

The treatment of choice for symptomatic cholelithiasis is laparoscopic cholecystectomy. Early referral for symptomatic patients may reduce the need for open cholecystectomy. All management should include a decrease in dietary fat.

Acute Appendicitis

The lifetime incidence of appendicitis in Western countries is about 7%, with about 200,000 appendectomies performed annually in the United States (4). Two-thirds of inflamed appendices are caused by obstruction, with fecaliths and calculi causing 10%. Complications of appendicitis occur in about 12% to 20%. While appendicitis mimics or is mimicked by other acute abdominal processes, certain features distinguish it. The rule is that symptoms *progress*, and do not fluctuate. The condition usually begins with pain in the periumbilical or epigastric area followed by anorexia, nausea, and indigestion. Pain is constant with occasional cramping. Within several hours the patient may vomit, and the pain will shift to the right lower quadrant, or to the right upper quadrant in cases of a long retrocecal appendix. Pain will be elicited on motion or coughing. Physical examination reveals point-tenderness in the right lower quadrant with rebound and referred tenderness in the same area, especially McBurney's point. Pelvic and rectal examinations should be done but are negative unless the appendix is pelvic or retrocecal. Helpful signs

of retrocecal appendix are the obturator sign (pain on internal and external rotation of the leg with knee and thigh flexed) (1) and iliopsoas sign (abdominal pain on flexing thigh against resistance of the examiners hand) (5). Bowel sounds are normal or slightly reduced. The body temperature may be slightly elevated at 37.8°C (100°F). A fever above 38.2°C (101°F) suggests perforation (6). In *situs inversus* the cecum and appendix may lie on the left side, mimicking diverticulitis. Laboratory findings include a white blood count (WBC) of 15,000 or more in 90% of patients, with 10% being between 10,000 and 15,000. In 75% of patients, the neutrophil count will be 75% or more. Urinalysis is usually normal with a few RBCs or WBCs seen in the urine in the case of pelvic or retrocecal appendicitis. Half of patients with acute appendicitis present with localized air-fluid levels, ileus, or increased soft tissue density in the right lower quadrant. Less common findings include a calculus within the appendix, altered right psoas shadow and right flank stripe. Use of ultrasound may increase the accuracy of the diagnosis. Findings of a noncompressible, aperistaltic appendix with a targetlike appearance in transverse view and a diameter of 6 mm or greater suggests acute appendicitis (7). Nonvisualization of the appendix does not exclude the diagnosis. Appendicitis is the most common nonobstetric emergency during pregnancy, complicating one in 1500 pregnancies (8). During pregnancy the appendix is displaced gradually toward the right upper quadrant. Infants with appendicitis may present with lethargy, irritability, and anorexia followed by vomiting, fever, and pain.

Complications of appendicitis include perforation, peritonitis, abscess, and pylephlebitis. Perforation manifests itself with more severe pain and fever above 38.3°C (100°F). Peritonitis is associated with increased tenderness, rigidity, abdominal distension, adynamic ileus, high fever and severe toxicity. An appendiceal abscess may be visualized by computerized tomography (CT) scan or ultrasound and treated by drainage, antibiotic therapy, or immediate appendectomy. Pylephlebitis is suppurative thrombophlebitis of the portal venous system accompanied by chills, high fever, mild jaundice, and hepatic abscesses. The condition can be prevented by aggressive antibiotic therapy given to patient with acute appendicitis who develops shaking chills. This can be detected by CT scan. Early diagnosis and prevention of perforation reduce morbidity and mortality.

The only treatment for appendicitis is surgical removal of the appendix, or surgical drainage and appendectomy if perforation has occurred. The latter is associated with great morbidity and significant mortality.

Gastrointestinal Obstructions

Incidents of gastrointestinal obstruction begin in the newborn period. Suspicion arises if the mother has prenatal polyhydramnios, more than 40 ml of fluid is aspirated from the infants stomach at birth, bilious vomiting and abdominal distention occur, and especially if no meconium is passed in the first 24 hours. Obstruction is caused by various types of atresias, stenoses, malrotations, and other anomalies.

Esophageal Atresia

The highest obstruction is esophageal atresia, which may or may not be associated with a tracheoesophageal fistula. Infants present early with choking, copious secretions, and if a fistula is present, cyanosis and respiratory distress. Diagnosis is made by placing an NG tube until resistance is met and taking a chest x-ray to determine the position of the tube.

Initial treatment consists of NG to continuous suction, intravenous fluids, and positioning the infant prone so less gastric reflux will enter the lung. Definitive treatment is surgical and is dependent on the length of the atresia. Closure of the fistula is essential. Anastomosis of the esophagus should be performed if possible. If not, a gastrostomy is done for feeding, and the esophagus repaired at a later date with a bowel or stomach graft if the distal and proximal segments of the esophagus cannot be brought together.

Pyloric Stenosis

Hypertrophic pyloric stenosis may present anytime from birth to 1 year of age, but most commonly between 2 weeks and 4 months. It affects males 4 times more than females. The symptom is vomiting, which becomes frequent and projectile. No bile is present in the vomitus, but blood may occasionally be found. Weight loss gradually occurs. Physical examination may reveal a peristaltic wave from the left costal margin toward the pylorus. A mass or "olive" may be palpated in the pyloric region if the infant is relaxed. If the wall

Thickness is greater than 4 mm and the length of the pylorus greater than 16 mm, it may be detected by abdominal ultrasound. If it is not seen but still suspected, a barium or Gastrograffin swallow will pick up the 8% of cases not seen on ultrasound. Diagnostic features include a string sign of the narrowed channel, a "beak" at the pyloric entrance, "shoulder" sign where the pylorus bulges into the antrum, the "tit" sign of contrast on the lesser curvature, and sometimes complete obstruction. The differential diagnosis includes feeding problems, intracranial lesions, achalasia, duodenal stenosis, malrotation of the bowel, and adrenal insufficiency. Complications of pyloric stenosis are dehydration, starvation, and hypokalemic hypochloremic alkalosis from persistent vomiting.

The preferred treatment is Fredet-Ramstedt pyloromyotomy. Preoperatively, an NG tube should be placed to drain the stomach and electrolyte imbalances corrected intravenously. Postoperatively, NG suction should be continued for 8 to 12 hours. Feeding should then be initiated with 10% dextrose solution in small amounts until tolerated, then advanced to regular formula (9).

High Intestinal Obstruction

This presents with early vomiting containing bile. In duodenal atresia, bile may be in the emesis. Bilious emesis implies midgut volvulus with bowel ischemia secondary to malrotation, or small bowel atresias, and thus demands immediate attention. Plain films should reveal dilated bowel, though gas may be seen distal to an incomplete obstruction. A barium or water-soluble contrast swallow should be done to reveal the position of the ligament of Treitz with respect to the level of obstruction and to exclude rotational deformity.

Treatment consists of NG suction, intravenous fluids, and respiratory support until it can be corrected surgically. Midgut volvulus requires emergency surgery, as blood supply to the gut is compromised. Atresias can be done electively.

Intussusception

This is the most common cause of bowel obstruction and of rectal bleeding in the child from 6 months to 2 years. It consists of a telescoping of bowel into an adjacent segment. Most commonly the terminal ileum telescopes into the right colon. The incidence

increases in midsummer and midwinter, and is associated with adenovirus infections. Other lead points include the Meckel's diverticulum, polyps, intramural hematoma, the appendix, and lymphomas, collectively accounting for the great majority of adult cases. The male to female ratio is 3:1. Eighty percent of cases are in children under the age of 2 years with a peak at 5 to 9 months, and seldom before 3 months. Symptoms begin with colicky bouts of abdominal pain, pallor and sweating causing the infant to cry. The bouts last about a minute. Reflex vomiting is an early sign, but reappears when the bowel obstructs. Blood and mucus in the stool produce a "currant jelly" appearance. A mass may be palpable in the abdomen, and is occasionally felt on rectal examination. The CBC usually reveals polymorphonuclear leukocytosis and hemoconcentration. The most important imaging examination is the barium enema, which shows the typical pattern of the obstruction and may even reduce the intussusception in about 50% of cases. The surgeon must be alerted to the suspicion of the diagnosis before attempting the barium enema in case it causes perforation. Complications of intussusception are progressive dehydration and edema, hemorrhage and ischemic infarction of the intussusceptum.

Treatment consists of fluid and electrolyte resuscitation prior to barium enema or surgery. Surgery is required when enemas have been unsuccessful or there are indications of perforation or peritonitis. The bowel may be manually reduced, but resection may be required, especially if the bowel is gangrenous.

Other Causes of Newborn Bowel Obstruction

Additional causes of distal obstruction in the newborn are meconium ileus, meconium plug syndrome, small left colon, Hirschsprung's disease, ileal atresia, and colonic atresia. A Gastrografin enema is not only diagnostic, but also a therapeutic tool in meconium plug syndrome, as it causes an osmotic diarrhea and passage of the plug. A high rectal atresia may be difficult to diagnose. The lowest obstruction is the imperforate anus, which can be detected in the newborn period by physical examination. This can be repaired surgically.

Small Bowel Obstruction in Adults

The most common cause of small bowel obstruction in adults is adhesions secondary to surgery or infection, especially pelvic in-

inflammatory disease. Other causes include hernias, neoplasms, foreign bodies, gallstones, inflammatory bowel disease, strictures, cystic fibrosis, and hematomas. Signs and symptoms depend on the level of obstruction. As in children, vomiting is early and profuse in high obstructions, late and feculent in lower obstructions. The amount of abdominal distention also varies from none in a high obstruction to moderate in a middle obstruction, and marked in a low one. All obstructions have intermittent pain, but the middle ones are classically crescendo and colicky. Physical examination will reveal normal to slightly elevated temperature, mild abdominal tenderness, and audible borborygmi. Initial laboratory values will be normal followed by leukocytosis, hemoconcentration, and electrolyte abnormalities as vomiting and dehydration progress. Serum amylase may be elevated. Classic x-ray findings include a ladderlike pattern of dilated small bowel and air-fluid levels. In select cases, the level and extent of obstruction can be determined by barium swallow with follow-through. Obtain a surgical consultation prior to ordering this examination.

A partial small bowel obstruction may be treated by decompression with a nasogastric or long intestinal tube (e.g., Miller-Abbott tube). An endoscope may be used to pass the tube through the pylorus. Sudden onset of shock, high fever, severe abdominal pain, rigidity and hematemesis may indicate strangulation of the bowel. Since this cannot always be diagnosed on clinical grounds, early surgical intervention is necessary. It is preferable to correct fluid and electrolyte imbalances and start antibiotics prior to operation.

Large Bowel Obstruction

Obstruction of the colon comprises about 15% of intestinal obstruction in adults. Complete obstruction is primarily due to neoplasms (65%), diverticulitis (20%), volvulus (5%), and miscellaneous other problems, including inflammatory bowel disease and fecal impaction. Symptoms depend on the competence of the ileocecal valve. Obstruction at the valve will cause symptoms of small bowel obstruction. An incompetent ileocecal valve will allow the pressure from a distal colonic obstruction to back up into the small intestine. A competent ileocecal valve will cause a closed loop obstruction with distention of the portion of the colon involved. High luminal pressure will impair circulation resulting in gangrene and perforation. Since the right colon has a

thinner wall than the left, it is more likely to perforate, and does so at about 10 to 12 cm diameter. A deep, crampy pain may be felt anywhere in the abdomen. A steady pain may indicate ischemia or peritonitis. Treatment is the same as for other bowel obstructions as detailed above.

Other Causes of the Acute Surgical Abdomen

Certain medical conditions of the bowel may develop surgical complications. These include diverticulosis and inflammatory bowel diseases such as Crohn's disease and ulcerative colitis. Diverticulosis is a condition of the bowel with multiple false diverticula. When the condition leads to diverticulitis and inflammation of the involved colonic segment, perforation and hemorrhage may occur. This happens when a diverticulum becomes infected and extends through the wall of the colon into peridiverticular tissues. This may be localized with a small perforation or generalized with a large perforation leading to peritonitis, abscess formation, and fistula formation. Diverticulitis most commonly presents in the left lower quadrant with acute constant and cramping abdominal pain, fever, and leukocytosis. When it occurs in the cecum, it resembles acute appendicitis. Pain and tenderness and sometimes a palpable mass are most commonly in the left lower quadrant or suprapubic area, but can be anywhere along the course of the colon. Bowel obstruction may be associated with the narrowed lumen produced by inflammation in the involved colonic segment. Patients may experience nausea, vomiting, and abdominal distention if significant obstruction is produced. Plain films may reveal free air from a perforation, an ileus, partial or complete obstruction, or a mass. Barium enema is contraindicated during an acute attack, but water-soluble contrast media may be used to evaluate the patient. Radiographic findings may include abscess cavities, sinus tracts, fistulas, and mass effects. Surgical treatment depends on the complication encountered and ranges from drainage of abscesses to colonic resection. Indications for immediate surgery are generalized peritonitis on admission to the hospital, hemorrhage, and failure of 3 to 4 days of medical therapy (see Chapter 13 for medical diagnosis and treatment).

Inflammatory bowel diseases also progress to varying degrees of perforation, hemorrhage, obstruction, abscess, and fistula formation. In these cases, the medical problem has usually been diagnosed. The important thing is to recognize when a surgical

complication occurs. The clinical presentations of each complication (hemorrhage, perforation, abscess formation, obstruction, and peritonitis) are classic, regardless of the underlying disease process. Surgery is directed toward each particular surgical complication, as mentioned above.

Unusual Causes of the Acute Surgical Abdomen

Meckel's Diverticulum. A Meckel's diverticulum may cause intussusception, diverticulitis, umbilical fistula, obstruction, abscess, or bleeding secondary to peptic perforation of ectopic gastric mucosa. More than half of patients with rectal bleeding secondary to this condition are under age 2. Bleeding is brisk, and the patient can exsanguinate quickly, so the patient must be operated on hastily. Pain of perforation of Meckel's diverticulitis mimics appendicitis. Cellulitis of the umbilicus is almost pathognomonic. The most common presentation in adults is intestinal obstruction. Technetium (Tc 99m pertechnetate) may localize in gastric mucosa revealing the Meckel's diverticulum. Retention of Tc 99m pertechnetate can be enhanced by giving 30 mg/kg of cimetidine intravenously 30 minutes before the scan.

All symptomatic Meckel's diverticuli and those with ectopic gastric mucosa should be resected.

Traumatic Ruptured Viscus. A viscus is any internal organ within a cavity. Organs of the gastrointestinal tract that may rupture are the esophagus, stomach, small intestine, colon, and rectum. Most traumatic ruptures are caused by accidents. It is important to get as much information as possible about the mechanism of injury. If the patient was in a vehicle, position in the vehicle, wearing of restraints, rate of speed and damage, such as a bent steering wheel, will help determine the nature and extent of possible injuries.

Esophagus. Traumatic rupture of the esophagus is extremely rare. Symptoms will include difficulty swallowing and pain on moving the head. Signs will be pneumomediastinum, pneumothorax, pleural effusion, fever, and chest pain. An esophagogram using water-soluble contrast will demonstrate only 30% of ruptures (10). Esophagoscopy may be needed for the definitive diagnosis.

Preoperative treatment consists of pain management, maintenance of blood pressure with crystalloid solution through a large-bore cannula, prophylactic antibiotics (penicillin 200,000 u/kg/d or clindamycin 40 mg/kg/d), and placement of a nasogastric tube

to suction. Repair consists of thoracotomy and operative closure of the defect. Antibiotics should continue postoperatively.

Stomach. Penetrating injuries of the stomach are more common than rupture by blunt trauma. As in other ruptures, an NG tube is placed and shock treated. Immediate laparotomy is necessary to control bleeding and repair the disruption. Antibiotics (cefazolin 50 to 70 mg/kg/d in 2 to 3 divided doses) are started before surgery and continued postoperatively.

Ruptures of the Intestines. Duodenal rupture may be difficult to diagnose due to lack of early symptoms. A CT scan of the abdomen should pick this up in patients with a history of blunt upper abdominal trauma. If not, and the condition is still suspected, an upper GI series with water-soluble contrast will demonstrate leakage. Treatment is as above for stomach rupture. Mortality and morbidity increase with delayed diagnosis.

Other parts of the small intestine are rarely injured with blunt trauma. Free air under the diaphragm may be noted on chest film. Treatment is as above for other ruptures.

Rupture of the colon and rectum cause a rapid peritonitis because of the large amount of bacteria that are spilled into the abdomen or retroperitoneal areas. A rectal examination must be done to look for injury. Check stool for gross and occult blood. Treat shock, start antibiotics, and proceed to laparotomy.

CANCERS OF THE GASTROINTESTINAL TRACT

Esophageal Cancer

In 1995 in the United States, 12,300 new cases of esophageal cancer were reported and 11,200 deaths (11). This cancer accounts for 4% of all gastrointestinal malignancies. It appears mostly between the ages of 50 and 60 and is more common in men than in women. Predisposing factors are thought to be heavy alcohol and tobacco use, achalasia, esophagitis and Barrett's esophagus. Both squamous cell carcinoma and adenocarcinoma are found in the esophagus. Rarer tumors include mucoepidermoid carcinoma and adenoid cystic carcinoma. These tumors invade locally and metastasize via the bloodstream and lymphatics. Distant metastases frequently go to liver, lung, bone, and adrenal glands. It presents with progressive dysphagia, weight loss, and anemia. Constant pain indicates invasion of other structures, and coughing

with swallowing may indicate a high lesion or development of a tracheoesophageal fistula. Hoarseness occurs when the cancer has spread to the recurrent laryngeal nerves. It can be diagnosed by barium swallow or direct esophagoscopy. CT scan of the thorax and abdomen must be done to evaluate lymphatic spread.

The only possible cure is surgery (10% to 15%). Radiation or chemotherapy can be used to shrink tumor mass before operation or for palliation in advanced cases.

Gastric Carcinoma

About 20,000 new cases of carcinoma of the stomach are diagnosed in the United States annually. The incidence is one-third of what it was 30 years ago. This may be due to changes in the prevalence of *H. pylori*, which is known to cause atrophic gastritis, a precursor for gastric carcinoma. The risk is proportionate to the serum levels of *H. pylori* antibodies. It is rare under the age of 40, and more common in men than women (2:1). Most gastric carcinomas are adenocarcinomas (95%). Squamous cell carcinomas usually invade the stomach from the esophagus. The earliest symptom is usually a postprandial feeling of abdominal fullness rather than pain. The patient has usually suffered dyspepsia in prior years. Next, anorexia develops with a special distaste for meat. Weight loss comes later. Vomiting occurs if pyloric obstruction is present. If the tumor is bleeding, the emesis may have a coffee-ground appearance. On physical exam a gastric mass may be felt in about 25% of cases. Hepatomegaly is present 10% of the time. Stool is usually positive for occult blood, with melena seen in some. Metastatic lesions arise in brain, bone, liver, and lungs. Metastases to the neck produce a Virchow node. The most prominent laboratory finding is anemia, in 40% of patients. The serum carcinoembryonic antigen (CEA) will be elevated in 65%. An upper GI study is adequate to diagnose most tumors, with a false-negative rate of 20%. An ulcerating tumor may look like a benign ulcer on upper GI. Gastroscopy should be performed when a new gastric ulcer is seen. It is accurate and allows multiple biopsies and cytology for definitive diagnosis.

Treatment consists of surgical resection. The extent of resection and reconstruction depends on the size and location of the cancer. The overall 5-year survival rate in the United States is about 2%. The 5-year survival rate according to stage ranges from 0% at stage IV to 70% in stage I. In stage I, the tumor has not penetrated

the serosa nor involved regional lymph nodes (12). By stage IV, the tumor has spread into adjacent structures and regional lymph nodes. Other tumors of the stomach include lymphoma and gastric pseudolymphoma, leiomyoma and leiomyosarcoma.

Cancers of the Small Intestine

Cancers of the small intestine make up less than 5% of gastrointestinal tumors or carcinomas (13). In 1995, 4600 new cases were reported in the United States, with 1140 deaths (14) with a mean age of onset of 59. The most malignant tumors of the small intestine are adenocarcinomas, leiomyomas, and lymphomas. Symptoms include pain, obstruction, bleeding, jaundice, and an abdominal mass. Diagnosis may be made on barium swallow with small bowel follow-through, or by endoscopy if high. Metastatic cancers in the small intestine include malignant melanoma and carcinomas of the breast, cervix, kidney, and lung. Adenocarcinomas and leiomyosarcomas should be resected if operable. If not, radiation therapy is used, which is also the treatment for lymphomas.

Carcinoma of the Colon and Rectum

Colon cancer is the second most common cancer in Western countries. In the United States, 133,500 new cases were reported and 54,900 deaths from colorectal cancer in 1995 (14). The incidence increases with age from 0.39 per 1000 per year at age 50 to 4.5 per 1000 per year at age 80. Carcinoma of the right colon is more common in women, and carcinoma of the left colon and rectum more common in men. Distribution of cancers of the colon and rectum are: 10% ascending colon, 12% transverse colon, 7% descending colon, 25% sigmoid, and 24% rectal (11). Adenocarcinomas make up 95% of colorectal cancers. People with familial adenomatous polyposis are at greatest risk for developing adenocarcinoma. Two other autosomal dominant hereditary nonpolyposis colorectal cancers (HNPCC) also have been identified and account for about 6% of patients with colorectal cancer. Patients with a first-degree relative with adenomatous polyps or colorectal cancer have a two- to threefold increased risk of colon cancer (15). Other conditions that predispose to colorectal cancer are ulcerative colitis, Crohn's disease, schistosomiasis, radiation exposure, polyps, and presence of a uretero-colostomy. Cancer of the colon and rectum are also associated

with environmental factors such as high fat and caloric intake, low dietary calcium, and decreased intake of fermentable fiber. Colorectal cancer spreads by direct extension, hematogenous, regional lymph node, transperitoneal, and intraluminal metastasis. Adenocarcinoma of the colon and rectum is slow-growing and is often present for 5 to 15 years before becoming symptomatic. Intuitively, one would expect to improve survival by detecting these cancers early, but few studies have been completed. Nevertheless, cumulative mortality from colon cancer was reduced by 33% over a 13-year period through screening for fecal occult blood (16).

The American Cancer Society recommends for screening: annual digital rectal examinations beginning at age 40, guaiac testing for occult blood annually after age 50, and flexible sigmoidoscopy every 3 to 5 years beginning at age 50. Screening of high-risk groups is less controversial: colonoscopy annually from age 25 or after 10 years of ulcerative colitis.

Symptoms depend on the location of the tumor in the bowel, size, and type of tumor, and complications (perforation, obstructions, hemorrhage). Cancer of the right colon often presents with unexplained microcytic hypo-chromic anemia, fatigue, weight loss, or a mass. Cancer of the left colon usually presents with changes in bowel habits, obstruction, and bleeding. Rectal cancer presents with hematochezia. Cancer must be ruled out as a cause of rectal bleeding in any middle-aged or older adult, even in the presence of hemorrhoids. Distal rectal cancers can be felt on digital exam.

Several other methods are available to detect colon cancer. The “gold standard” is colonoscopy, which allows the entire colon to be examined by direct visualization. Approximately 20% of colorectal cancers are visible with the rigid sigmoidoscope, 30% to 40% with the 30 cm flexible sigmoidoscope, and 50% to 65% with the 60 cm sigmoidoscope. Barium enemas are important in diagnosing colon cancers. Lesions of the left colon often appear as an “apple core” lesion, whereas tumors of the right colon appear as masses or a constriction. CT scans are helpful in detecting metastatic lesions in the liver or local extension of rectal cancer. MRI may also be useful for the latter. Chest x-rays should be done to look for metastatic lesions. CEA is a glycoprotein present in many tissues, but especially cancers of the GI tract. Though CEA is elevated in 70% of patients with colon cancer, less than half of patients with localized disease are positive, so it is not a useful screening tool for colorectal cancer. It is used more to follow for cure after resection.

In stages B, C and D, patients are given chemotherapy, conferring significant improvements in survival. Staging of this cancer is useful because of its ranking incidence and because of correlations between stage at the time of diagnosis and 5-year survival. Duke's stages' definition and corresponding survival rates are as follows:

Stage A—limited to mucosa and submucosa — 90%

Stage B—extending into muscularis or serosa -- 60%–75%

Stage C—involving regional nodes — $\leq 59\%$

Stage D—metastases to liver, bone, lungs — 5%

Treatment for carcinoma of the colon is surgical resection. Resection of a rectal tumor depends on its position and extension and usually requires a permanent colostomy. Other therapies include fulguration (electrocoagulation), laser photocoagulation, radiation, and chemotherapy. Complications of colorectal cancer are obstruction, perforation, and direct extension.

Other Neoplasms of the Bowel

Other neoplasms of the bowel include carcinoids, lymphomas, lipomas, leiomyomas, and endometriomas. Carcinoid tumors occur mostly in the rectum. They can cause local symptoms or metastasize, and cause carcinoid syndrome in 5%. The most common noncarcinomatous malignancy of the colon is lymphoma. Two AIDS-related cancers that affect the colon and rectum are non-Hodgkin's lymphoma and Kaposi's sarcoma. Lipomas are benign but may cause obstruction. Leiomyomas are less common in the bowel than the stomach but may cause hemorrhage or become malignant. Endometriomas may cause rectal bleeding during menstruation. Other benign tumors include neurofibromas, teratomas, enterocystomas, lymphangiomas, and cavernous hemangiomas. Intestinal lesions are excised or the segment resected.

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Diseases of the Liver

Joseph J. Nidiry

ACUTE HEPATITIS

About 90% of patients with liver disease present with acute illness, with jaundice, signs of hepatocellular injury, or both. The most common causes of acute hepatocellular injury are viruses or toxins. Patients with acute inflammation and destruction of the hepatic parenchyma present to physicians with signs ranging from fatigue to coma. Evaluation of patients with acute hepatitis requires attention to historic features such as exposure to blood or blood products, intravenous drug use, exposure to toxins, medications the patients are using, foreign travel, sexual practices, and exposure to individuals with hepatitis. Viruses cause hepatocellular disease by causing damage directly or through immune mediated mechanisms.

Viral Hepatitis

The severity of symptoms varies from subclinical illness to fulminant hepatitis leading to coma. Many viruses cause hepatitis, but only 5 and possibly 6 well-defined hepatotropic viruses have been characterized by molecular technology. The agents are called hepatitis A, B, C, D, E, and G viruses. No detailed information is available about G virus except that it is associated with transfusion. EB virus, CMV, herpes, varicella, adenovirus, and some other rare pathogens should be excluded if clinically indicated.

Hepatitis A Virus (HAV)

It has a fecal-oral transmission caused by an RNA virus that causes acute, but not chronic, hepatitis. The infection is usually acquired

subclinically and is seen in the developing world, where it can assume epidemic proportions. The infection is acquired usually in childhood, but with improving standards of hygiene and sanitation, it is increasingly less likely in developed countries. Because of this phenomenon, clinically evident infection in young adults is seen more frequently. An estimated 30 million individuals from developed countries travel to endemic areas, and a large number of them are at risk for contracting this infection.

Often the infection is subclinical, with clinical hepatitis occurring in a minority of patients. Fulminant hepatic failure is rare and carries a better prognosis with HAV than with other viruses. Atypical clinical variants include cholestatic hepatitis and relapsing hepatitis. Other atypical manifestations include leukocytoclastic cutaneous vasculitis, arthritis, and cryoglobulinemia, which are extrahepatic and most likely related to immune complex phenomena.

Both cytopathic and immunopathogenetic mechanisms may play a role in hepatocellular necrosis due to the hepatitis A virus. The diagnostic test of acute HAV infection is presence of IgM anti-HAV antibodies. An IgG antibody denotes past infection. An inactivated hepatitis A vaccine has been licensed in the United States and has been shown to be immunogenic in 99.8% of individuals after two doses.

Hepatitis B Virus (HBV)

Approximately 300,000 new cases of acute Hepatitis B are estimated to occur annually in the United States. Five percent to ten percent of infections acquired in adult life progress to varying severities of chronic hepatitis and some into cirrhosis.

Evidence thus far indicates that HBV is not directly cytopathic, and hepatic necrosis and subsequent clearance of the virus are mediated via the host immune system. Diagnosis of HBV infection largely relies on the presence of a hepatitis B surface antigen (HBsAg). Acute and chronic infections are distinguished by the presence of IgM and IgG antibodies to the inner hepatitis B core protein (anti-HBc). Acute HBV infection in the absence of HBsAg positivity (anti-HBc IgM positivity in the "window period") is theoretically possible but rare. Presence of IgM anti-HBc indicates recent infection, although this marker may occasionally be present during acute reactivation of chronic infection. Hep-

hepatitis Be antigen (HBeAg) is a cleaved protein product of the hepatitis B core gene, which is indicative of active HBV replication. Antibodies to HBeAg (anti-HBe) are present in inactive or non-replicative HBV infection. Actively replicating mutant viruses ("precore" mutants), with detectable HBV DNA in serum, have been reported in both acute and chronic HBV infection in the absence of HBeAg (anti-HBe positive). Antibodies to the hepatitis B surface antigen (anti-HBs) indicate vaccine-induced immunity; antibodies to both core and surface proteins (anti-HBc and anti-HBs) indicate prior HBV infection. Interpretation of isolated anti-HBc (IgG) positivity is problematic since this may represent ongoing, low-level HBV infection, prior HBV infection, or a false-positive test. Typically, anti-HB IgM is indicative of acute HBV infection and anti-HB IgG indicative of resolving HBV infection. On occasion, acute flares of chronic HBV are associated with anti-HB-core IgM positivity.

Both plasma-derived and recombinant yeast-derived vaccines are immunogenic and safe. An anti-HBs titer of over 10 mU/mL is considered "protective." Vaccine is administered intramuscularly according to a schedule (Table 15.1). An accelerated regimen, i.e., 0, 1, 2, and 12 months, may be ideal in certain high-risk individuals, particularly neonates born to HBsAg positive mothers. The current CDC strategy is to incorporate hepatitis B vaccines in the pediatric immunization schedule. This is because HBV infection in children carries a higher risk of chronic hepatitis.

The course of chronic hepatitis B may be characterized by biochemical (high alanine transaminase [ALT], aspartate transaminase [AST], and bilirubin) and clinical (ascites and encephalopathy) flares, and these may be due to one of several reasons: superimposed hepatitis (viral, drug, or alcohol) HBeAg seroconversion or spontaneous reactivation. Clinical and serologic evaluation would help identify the problem.

Alpha interferon (alpha-IFN) has been effective in clearing HBeAg and HBV-DNA in approximately 40% of patients after 5 million units SC daily for 4 months. Furthermore, HBsAg clearance has been noted in approximately 10% in the immediate follow-up period. With longer follow-up of up to 6 years, 65% have been observed to clear HBsAg. Careful selection of patients may improve the results. Favorable prognostic features for response to INF include female gender, Caucasian race, disease acquired in adult life, HIV-negativity, heterosexual lifestyle, absence of

Table 15.1.
Recommended doses of currently licensed hepatitis B vaccines.

Group	Recombivax HB ^a		Engerix-B ^a	
	Dose (μg)	(mL)	Dose (μg)	(mL)
Infants of HBsAg-negative mothers and children < 11 years	2.5	(0.5) ^b	10	(0.5)
Infants of HBsAg-positive mothers; prevention of perinatal infection	5	(0.5) ^c	10	(0.5)
Children and adolescents 11–19 years	5	(0.5) ^c	20	(1.0)
Adults ≥ 20 years	10	(1.0) ^c	20	(1.0)
Dialysis patients and other immunocompromised people	40	(1.0) ^d	40	(2.0) ^e

^aBoth vaccines are routinely administered in a 3-dose series. Engerix-B also has been licensed for a 4-dose series administered at 0, 1, 2, and 12 months.

^bNew pediatric formulation.

^cPreviously licensed formulation; may be used to deliver the appropriate age-specific dosage to infants of HBsAg-negative mothers and children < 11 years.

^dSpecial formulation.

^eTwo 1.0-mL doses given at one site, in a 4-dose schedule at 0, 1, 2, 6 months.

Health Information for International Travel, 1995. U.S. Department of Health and Human Services, Public Health Service.

delta infection, greater hepatocellular necrosis noted histologically, high pretreatment ALT and low pretreatment HBV-DNA.

In the responder to alpha-IFN, most often an early rise in transaminase (biochemical flare) because of an enhanced cytotoxic T-cell activity and natural killer (NK) cell activity is noted. Therefore, alpha-IFN is not to be used in decompensated liver disease.

The response to IFN is sustained with loss of HBV-DNA and HBeAg, with delayed clearance of HBsAg. Hepatic biochemical tests normalize in most patients (approximately 80%) with improvement in histologic activity. A few have been noted to have HBV-DNA by PCR, the significance of which is unclear.

Thymosin-alpha, in a preliminary trial, has been noted to be effective in treating chronic hepatitis B infection. Thymosin-alpha is a hormone-like polypeptide synthesized by recombinant techniques and has immunomodulatory functions. A large trial in treating chronic HBV infection is ongoing, and the results are

gerly awaited. An advantage of this treatment over IFN is fewer side effects.

Liver transplantation has been done in chronic B hepatitis, but this continues to be a controversial area. Despite the use of hepatitis B vaccines, anti-HBs preparations and alpha-IFN, HBV recurrence has been seen in most patients. Recurrence in HBeAg (+) chronic HBV infection and in fulminant hepatic failure is also common. Long-term mortality beyond 2 months has been observed to be significantly worse in HBsAg-positive transplanted individuals, in whom a high incidence of graft dysfunction has also been noted.

Hepatitis C Virus (HCV)

Using sophisticated molecular biology techniques, an epitope of hepatitis C virus (HCV) was cloned in 1989. Through validation studies, it has been determined that HCV is responsible for most cases of previously diagnosed parenterally transfused non-A, non-B hepatitis. HCV has been determined to be a lipid-enveloped RNA virus, approximately 50 nm in diameter. It is classified as a flavilike virus sharing nonstructural genomic homogeneity with human flavi and animal pestiviruses.

Serologic studies for hepatitis C continue to be in a state of constant evolution. The first licensed assay was anti-HCV by ELISA, and this tested for an antibody against c100-3 epitope of C virus. This test is seldom positive in the acute phase of hepatitis C and is a “window” between onset of symptoms and appearance of anti-HCV, with 60% becoming positive in 4 months and 90% in 6 months. Seroprevalence of this first-generation anti-HCV in intravenous drug users and hemophiliacs is 60% to 90%, in dialysis patients is 15% to 20% and is approximately 0.6% to 1.2% among blood donors. The first-generation test has high false positivity and has been noted in alcoholic liver disease, primary biliary cirrhosis, cryptogenic cirrhosis and “autoimmune” hepatitis.

A second-generation anti-HCV, by ELISA, was recently approved by the FDA and is available commercially. This test, which replaced the first-generation anti-HCV, probes for antibodies against three viral proteins, c22-3 (a structural protein), and c100 (a composite antigen of c100-3 and c33c). The use of additional antigens has increased the detection of true-positive among high-risk groups such as hemodialysis patients, intravenous drug abusers and hemophiliacs by 5%, to 40%. In acute

posttransfusion or sporadic hepatitis, increased detection in 20% of cases has been noted. Additionally, second-generation assay has detected anti-HCV in cases of acute hepatitis 30 to 60 days earlier than detection by first-generation assay.

Recombinant immunoblot assay (RIBA-II) is a supplemental assay that incorporates four of the, thus far, cloned epitopes of hepatitis C virus (5-1-1, c100-3, c22-3, and c33). RIBA reactive blood donors, when evaluated retrospectively, had high infectivity and readily transmitted (approximately 80%) non-A, non-B (NANB, HCV) hepatitis. RIBA-II can diagnose hepatitis C infection in at least 10% more patients that had clinical evidence of chronic C hepatitis and were first-generation ELISA anti-HCV (-). HCV-RNA, detected by PCR, is a sensitive assay. This, however, needs expertise and is labor intensive, and at the present time is confined to research laboratories.

Sexual transmission of hepatitis C infection may occur in promiscuous heterosexuals and homosexuals, but certainly less efficiently than with HBV and HIV. A coinfecting hemophiliac with HCV and HIV has been noted to transmit more readily HCV, as compared with an individual with HCV infection alone. In a stable monogamous relationship, risk of HCV transmission is low. HCV-RNA by PCR has not been noted in human secretions such as semen, saliva, breast milk, or vaginal mucus. Perinatal transmission has not been proved conclusively except in the case of mothers coinfecting with HCV and HIV. Studies thus far have not shown an etiologic relationship between HCV and sporadically occurring fulminant NANB hepatitis. Estimated incidence of postneedle-stick hepatitis C infection has been shown by one study to be 4%, compared with a 67% incidence of HBV infection following needle-stick exposure to an HBeAg-positive case.

The present estimated incidence of post-transfusion HCV hepatitis is about 3%. Approximately 50% of patients with acute HCV hepatitis progress to chronic hepatitis.

HCV has genomic heterogeneity. Different isolates have been reported from the United States, Japan, and Europe, based on the published reports on genomic sequences of HCV-I, HCV-II and HCV-III. Clinically multiple infections of varying severity may occur due to the different strains, and their diagnosis presents difficulties. The genomic variation of HCV may also present problems in vaccine development. Hepatitis C-related hepatocellular carcinoma (HCC) is being reported with increasing frequency.

Alpha-IFN is an approved drug for the treatment of chronic hepatitis C. Approximately 50% of patients respond to a dose of 3 million units 3 times a week for 6 months; however, half of these patients relapse upon discontinuation. In the responder, normalization of transaminases occurs within the first 12 weeks. Higher doses for better response are being evaluated. Maintenance regimen for relapses will have to be addressed in the future. HCV-RNA by PCR has been noted to decrease in responders to alpha-IFN (as defined by normalization of transaminases). Relapses have been more frequently associated with reappearance of persistence of HCV-RNA.

Recurrence of hepatitis C infection has been observed in less than 15% of patients following liver transplantation. However, using PCR to detect HCV-RNA, it has been shown that more than 5% of patients redevelop a viremic state if they were HCV-infected pretransplant. Clinically significant chronic hepatitis may occur in one-third of the patients. A lot still must be learned regarding the course of HCV infection in transplantation.

Hepatitis E Virus (HEV)

This enterically transmitted infection is endemic to various geographic areas outside the United States. The genome of hepatitis E virus RNA has been cloned, and preliminary evaluation of serologic assays for both acute and past infection are underway. Clinically, this infection, to a large extent, resembles hepatitis A with no known chronicity. An important clinical difference from acute A hepatitis is the 20% mortality rate among infected pregnant women, particularly in their third trimester.

Hepatitis D Virus (HDV)

Delta (D) hepatitis is caused by an incomplete RNA virus that requires hepatitis B virus for replication and expression. It is usually associated with a progressive or more aggressive course of hepatitis B (fulminant hepatitis, chronic active hepatitis). HDV infection forms two distinct patterns. In endemic areas such as the Mediterranean countries, transmission is by nonpercutaneous means; in nonendemic areas, it is through percutaneous routes. HDV infection can occur only in the presence of HBV infection. Therefore, delta infection can occur where a simultaneous coinfection with viruses exists or when a superinfection with

HDV occurs in someone who is already infected with HBV. Diagnosis of D infection is based on detection of the presence of antibody to HDV, or delta antigen in liver tissue, or HDV RNA in serum. Preventing hepatitis B should prevent hepatitis D.

Management of Viral Hepatitis

Most patients with acute viral hepatitis recover without sequelae. Patients should be hospitalized if they have prolongation of prothrombin time, evidence of encephalopathy, ascites, or dehydration from vomiting. Bed rest has been recommended; however, it has not been shown to shorten the duration of disease. A high-calorie, high-protein diet may shorten the duration of illness.

Liver Injury Caused by Drugs and Chemicals

Liver damage from drugs and toxic exposure is the second common cause of acute hepatitis and a leading cause of chronic liver disease. Drug reactions affecting the liver can have many manifestations, from asymptomatic elevation of the transaminases to acute fulminant hepatic necrosis. The mechanisms of drug-induced damage fall into two broad categories: direct hepatocellular injury and idiosyncratic hepatotoxicity. Either the parent drug or its metabolite can cause injury. Oxidation of radicals is the most common pathway responsible for toxic products from drug metabolism. Hepatocellular injury, cholestasis, vascular injury, and neoplastic process all can occur from hepatotoxins. A representative table of types of injury and examples of drugs is shown in Table 15.2. It is in no way a complete list, and when questions arise, further review of appropriate literature is indicated.

Alcoholic Liver Disease

Alcohol is the most common cause of drug-induced liver injury. Unlike with most other drugs, liver damage develops with long-term use of alcohol, not short-term use. The risk of liver damage is high in men who drink more than 60 to 80 gm of alcohol per day (4 to 6 drinks). Women are more susceptible to alcohol damage than men and have a lower threshold, 40 to 60 gm. Ethanol can also aggravate preexisting liver disease. Increased mortality in patients with hepatitis C and α_1 -antitrypsin deficiency has been reported. Alcohol appears to potentiate the hepatotoxic effect of other substances such as acetaminophen and carbon tetra-

Table 15.2.
Drug-induced liver injury.

Type of Injury	Example of Responsible Drugs
Hepatocellular injury	
Acute necrosis	Acetaminophen, carbon tetrachloride
Acute hepatitis	Isoniazid, aspirin, phenytoin
Chronic hepatitis	Isoniazid, a-methyldopa, nitrofurantoin
Fatty liver, steatohepatitis	Tetracycline, valproate, corticosteroids, nucleoside analogs, ethanol, amiodarone
Cholestasis	
Inflammatory	Chlorpromazine, erythromycin, amoxicillin-clavulanate
Noninflammatory	Oral contraceptives, rifampin
Granulomatous inflammation	Allopurinol Quinidine
Vascular injury	
Peliosis hepatitis	Anabolic steroids, oral contraceptives
Hepatic vein thrombosis	Oral contraceptives
Porto-occlusive disease	Antineoplastic agents
Tumors	
Hepatic adenoma	Oral contraceptives
Hepatocellular carcinoma	Anabolic steroids
Angiosarcoma	Vinyl chloride

chloride. Genetic susceptibility may play a role in the development of alcoholic liver disease, as only 15% of alcoholics develop alcoholic liver disease.

Alcoholic liver disease has three broad categories: fatty liver, alcoholic hepatitis, and cirrhosis.

More than a third of heavy drinkers have fatty liver that is occasionally associated with elevation of transaminase. Gamma glutamyl transpeptidase (GGT) is more sensitive than ALT and AST. GGT can also be elevated even in a nonalcoholic who has ingested significant amounts of ethanol in the previous 48 hours. However, abnormalities return to normal after abstinence. Alcoholic hepatitis is a clinical and pathological entity that denotes occurrence of irreversible damage unless the patient abstains from alcohol.

The clinical syndrome is characterized by jaundice, anorexia, right upper quadrant pain, nausea, and vomiting. Many have fever, and some may present with ascites and encephalopathy. Many patients have leukocytosis and elevated bilirubin. The characteristic finding, however, is AST (SGOT) twice the value of ALT (SGPT), and AST elevation is usually below 200 IU. GGT is almost always elevated. The pathology is characterized by hepatocellular necrosis, steatosis, polymorphonuclear infiltrates, and Mallory bodies.

Many of the synthetic functions of the liver may be compromised (e.g., low albumin, low cholesterol, low prothrombin). Alcoholic hepatitis almost invariably progresses to cirrhosis if patients continue to drink, as it will in 20% to 25% of patients even after abstinence.

Management consists of abstinence, and nutritional and vitamin supplementation. Short-term mortality from severe alcoholic hepatitis has been reduced by use of corticosteroids. Cirrhosis will be discussed later.

Chronic Liver Disease

Chronic liver disease evolves over months to years and may be manifested only by abnormal laboratory values. Chronic liver disease could be a result of inherited liver disease, hepatitis, or an autoimmune process.

Inherited Liver Disease

Alpha₁ – Antitrypsin Deficiency: Diagnostic criteria are presence of liver disease with a low serum antitrypsin level, no alpha peak on serum protein electrophoresis, and an abnormal Pi phenotype. Liver disease occurs in infancy and is the most common metabolic cause of liver disease in children and the most common metabolic disease for which children undergo liver transplantation. Onset of symptoms and rapid deterioration are somewhat characteristic. In some patients pulmonary involvement leads to emphysema. No treatment is available; liver transplantation indicated.

Hemochromatosis

Inherited as an autosomal recessive trait, primary hemochromatosis is the most common genetic liver disease. Associated involvement of other organs with diabetes, heart failure, arthritis, and impotence may present before signs of liver involvement. Diag-

sis is made by a finding of serum iron saturation of transferrin of more than 62% in men and 75% for premenopausal women, and elevated ferritin level. High tissue iron level can be demonstrated on liver biopsy. Patients should be treated with repeated phlebotomies or chelation therapy.

Wilson's Disease

Wilson's disease is an autosomal recessive disease that results from inability of liver to excrete copper in the bile. Copper thus accumulates in the liver, CNS, cornea and kidneys, causing the clinical manifestations. Neurological symptoms are those of basal ganglion involvement. The Keyser-Fleisher ring is characteristic, and hemolysis and renal tubular acidosis are common. Low ceruloplasmin level, high serum copper and increase in urinary copper are classical findings. Patients should receive the chelating agent Pencillamine, most often for life.

Autoimmune Liver Disease

Primary Biliary Cirrhosis (PBC)

This disease, which occurs predominantly in Caucasian women, is due to autoimmune destruction of the small bile ducts. Biochemical abnormalities of elevated alkaline phosphatase and cholesterol precede clinical symptoms by many years. Pruritis, xanthomas and symptoms of cholestasis, or portal hypertension may be presenting features. Fat and fat soluble vitamin malabsorption are common. Antimitochondrial antibody anti-M₂ is specific for the disease and is present in 95% of patients. Liver biopsy and endoscopic retrograde cholangiopancreatography (ERCP) will support diagnosis. Immunosuppressant therapy has not been very promising. Liver transplantation is the treatment of choice.

Primary Sclerosing Cholangitis (PSC)

In contrast to primary biliary cirrhosis, both intra- and extrahepatic biliary systems are involved in sclerosing cholangitis. Sixty percent of patients have associated inflammatory bowel disease. Unlike primary biliary cirrhosis, antimitochondrial antibodies are not present. Patients with AIDS develop a biliary tract disease from cryptosporidium with clinical characteristics similar to PSC. ERCP is diagnostic. Patients develop recurrent attacks of bacterial

cholangitis, which usually respond to antibiotics. Ten percent of patients with PSC develop cholangiocarcinoma. Liver transplantation should be considered in patients with PSC.

Autoimmune Hepatitis

Accounting for about 10% of chronic liver disease, 75% of patients with this disease are women under age 30. The disease has insidious onset and is diagnosed by elevated transaminase levels and exclusion of other causes. Many autoantibodies are found in autoimmune hepatitis. All patients have hyperglobulinemia. Type I has antinuclear (ANA) and antismooth muscle antibodies (SMA). Type II has anti-liver-kidney microsomal antibodies (anti LKM-I) but no ANA or SMA. Type III has no ANA or SMA but anti-soluble liver antigen antibodies. Liver biopsy reveals plasma cell infiltration of the liver. It is important to make an early diagnosis, as treatment with corticosteroid is very effective. Azathioprine is also effective.

Hepatic Effects of Systemic Disease

Granulomas involving liver are found in conditions in which granulomatous reaction occurs elsewhere. Sarcoidosis and TB are the most common causes, but fungal infections (e.g., histoplasmosis) viral (CMV) and other rare causes (syphilis) must be sought for.

Budd-Chiari syndrome is due to occlusion of hepatic veins. Hypercoagulable conditions and oral contraceptives are the most common underlying causes in the United States. Liver function tests are usually normal; patients, however, develop massive ascites and hepatomegaly.

Schistosomiasis is the most common cause of portal hypertension in the world. The disease develops from the eggs of *Schistosoma mansoni*, which lodge in the portal vein, causing occlusion and fibrosis. Patients develop portal hypertension with little liver function abnormalities. Active infection can be treated with praziquantel.

Nonalcoholic steatosis is due to fatty infiltration in the liver seen mostly in patients with obesity, diabetes, hyperlipidemia, total parenteral nutrition (TPN), and jejunio-ileal bypass. Usually patients have mild elevation of aminotransferase levels. Weight loss and correction of metabolic abnormalities, when relevant, such as control of diabetes, will result in resolution of abnormalities.

Cirrhosis

The end result of chronic liver injury is necrosis of the liver cells and replacement with fibrous tissue resulting in cirrhosis. Clinical manifestations are due to decreases in the normal functions of the liver, especially synthetic functions, and development of portal hypertension because of distortion of the liver architecture. Patients with cirrhosis develop two distinct clinical syndromes: portal hypertension and hepatic failure.

Portal hypertension typically presents with development of ascites and esophageal varices. Paracentesis fluid should be examined for protein, glucose content, amylase, blood cell count, bacterial fungal and AFB cultures, pH and cytologic examinations. A ratio of serum albumin to ascitic fluid protein of 1:1 suggests portal hypertension. A ratio below suggests nonhepatic disorders in patients with ascites and liver disease. Ascites should be treated initially with salt restriction and spironolactone. Only in refractory cases should loop diuretics be added. Treatment of underlying liver disease and high protein diet will also help in reducing the ascites. Repeated therapeutic paracentesis of large volume has been recommended in patient with massive ascites and low sodium excretion (<10 mEq) in urine. Peritoneojugular shunt (Le Veen) is effective, though it is associated with many complications, which have limited its use.

Spontaneous bacterial peritonitis is a complication of ascites in about 5% of patients. Fever, leukocytosis, abdominal pain, and tenderness are classical signs. Ascitic fluid is cloudy with more than 300 wbc/mL with predominance of neutrophils and a pH below 7.35. Grams stain is positive in only 25% of patients. Patients should be treated with broad spectrum antibiotics to cover both Gram-positive and Gram-negative organisms.

Hepatorenal syndrome is reversible renal failure associated with severe liver disease. It may be precipitated by vigorous diuresis, hemorrhage, or infection. Urinary electrolytes showing normal urine osmolarity with very low sodium (less than 5 mEq/L) is characteristic. Prognosis is poor.

Variceal bleeding is the most dreaded complication of portal hypertension. Mortality from bleeding is still 30%. Diagnosis is made by endoscopy. Treatment for variceal bleeding is pitressin infusion with or without nitroglycerin and endoscopic sclerotherapy or banding. Survival of patients seems to have improved from these treatment modalities. Patients with documented varices will also

benefit from beta-blocker therapy in the prevention of bleeding by decreasing portal hypertension.

Hepatic Failure

Hepatic encephalopathy is a complex neuropsychiatric disorder developing when toxins escape into the systemic circulation because of impaired hepatic clearance in acute and chronic liver disease. The condition is characterized by disturbances in consciousness, personality, behavior, and neuromuscular function. Early manifestations include reversal of the normal sleep pattern, hypersomnia, irritability, forgetfulness, and neglect of personal hygiene. Psychomotor apraxia and asterixis are present in most. The most common laboratory abnormalities found in patients with encephalopathy are elevated ammonia and CSF glutamine levels and low levels of branch chain aminoacids in the sera. Electroencephalogram shows nonspecific slow wave activity. Important precipitating factors for the development of encephalopathy are increased protein intake, sedative and analgesic drugs, infection, gastrointestinal bleeding, hypokalemia, azotemia, and hypovolemia.

Crucial in the treatment of hepatic encephalopathy is identification and treatment of the precipitating factors (e.g., electrolyte aberration, infection), lowering the ammonia level with decreasing protein intake, cleansing of the GI tract of nitrogenous material (blood). These may result in improvement of mental status. The physician should exclude other causes of encephalopathy, especially subdural hematoma, hypoglycemia, meningitis, and sedative overdose.

Nonabsorbable antibiotic treatment to sterilize the gut (e.g., neomycine) has been the treatment of choice for encephalopathy. Currently, however, lactulose is the most important drug available for treating patients with hepatic encephalopathy. The drug can be given orally or by enema. Dosage should be adjusted for individual patients to achieve 3 to 4 BM per day.

Encephalopathy occurring in acute hepatitis does not respond to these measures. Cerebral edema seems to be the underlying problem in those cases, and appropriate therapy is indicated. Coagulopathy occurs in hepatic failure, and administration of coagulation factors as needed is important in sustaining life in many patients with hepatic failure.

Problems of the Urinary Tract

Chapter 16

Urinary Tract Infections

Kurt Kurowski

URINARY TRACT INFECTIONS (UTIs)

itis is common among adult females, with approximately 50% of women experiencing at least one episode during their lifetimes. This contrasts with the male population, in whom cystitis is rare. The decreased incidence in males is secondary to their longer urethras, which makes bacterial ascension more difficult. Secretions also have some bacteriostatic properties. The exceptions to this occur at the extremes of life. In infants (age <1 yr), UTIs are more common in males than females. Uncircumcised male infants are at a greater risk (1). The mucosal opening of the foreskin may serve as an attachment site for fimbriated bacteria. The incidence of UTIs also increases in the elderly population (although women are still more commonly affected). This is secondary to the increased incidence of benign

prostatic hypertrophy and prostatic carcinoma in this age group, with prostatic urethral obstruction, urinary retention, and stasis. UTIs in children are fairly common, with about 1% of boys and 4% of girls developing infection. Most of the infections in girls occur when they are older. As girls age, they gradually take on the propensity for UTIs of their adult female counterparts.

PATHOPHYSIOLOGY

Urinary tract infections usually occur through ascension of bacteria up the urethra. Sexual intercourse provokes this in some women. The use of a diaphragm also increases the risk for infection. For a bacterial species to be pathogenic for the urinary tract, it must be located near the urethra. Fimbriated bacterial subtypes that can adhere to urinary tract epithelial cells are more prone to produce cystitis and upper urinary tract infections, of particular pertinence to UTIs and uropathogenic *E. coli*. Obstruction to the proper flow and voiding of urine promotes infection, as occurs with duplicated ureters, medullary sponge kidney, horseshoe kidney, ureteral stone, and a faulty ureterovesicular valve mechanism. In women with frequent cystitis, enteric organisms often have replaced the normal lactobacillus colonization of their vaginal mucosae. This is believed to be secondary to genetic differences in receptors in their uroepithelial cells and correlates with certain HLA and blood group antigens (2, 3, 4). The low pH, high osmolarity and urea content of urine make it bacteriocidal. The bladder mucosa has a mucin coating that inhibits bacterial adherence. Instrumentation of the urinary tract (including catheterization) not only physically transports vaginal or periurethral organisms into the bladder, but also may disrupt the protective mucin coating and the underlying mucosa. Even a single insertion of a catheter produces a 1% UTI incidence (5). The geriatric population has a higher incidence of asymptomatic bacteriuria and UTIs, believed secondary to poor bladder emptying, perineal soiling in women, and partial prostatic urethral obstruction in men. Patients with diabetes mellitus are more prone to asymptomatic bacteriuria and UTIs as well as severe complications, including papillary necrosis. Ureteral stones can be associated with UTIs in several ways. They produce not only obstruction to urine flow, but also mucosal injury and loss of mucin protection. Struvite stone formation can be a result of UTI if the organism is of a urea splitting variety (*Proteus mirabilis*, *Ureaplasma urealyticum*, others).

CYSTITIS

Clinical Presentation

The patient may complain of dysuria, urinary frequency, and urinary urgency. The likelihood of a UTI being responsible for the patient's symptoms increases if more than one of these complaints is present. Burning throughout the entire course of urination sometimes helps to identify patients with cystitis (versus patients with urethritis, who may complain of pain only with the start of urination), but most patients have difficulty describing this difference. Some patients may notice some minor suprapubic pain and/or have a low-grade fever, but most patients with cystitis have neither of these.

The patient appears comfortable unless she has to urinate and is usually afebrile. No costovertebral angle (CVA) tenderness will be present. Mild suprapubic tenderness without guarding or rebound is sometimes elicited.

Urine analysis will reveal a positive leukocyte esterase on dipstick and if examined microscopically, will reveal >5 to 10 white blood cells per high-power field. Urine dipstick for nitrite is specific but only about 30% sensitive for UTI. It relies on the ability of some of the subtypes of most of the typical urinary pathogens to convert urine nitrate to nitrite. (*Staphylococcus saprophyticus* is unable to produce this conversion.) It is considerably more sensitive (about 60%) if urine is voided just after awakening to allow several hours of incubation. In contrast to patients with acute or subclinical pyelonephritis, most adult patients with cystitis do not require urine cultures. Exceptions are in cases in which the potential for more resistant organisms exists, such as in patients with previously mentioned risk factors or hospital or nursing home patients, or those who have not responded to empiric therapy directed against the most likely causative organisms.

E. coli remains the predominant infecting organism in these patients, but a higher percentage of infections from *Enterococcus*, *Pseudomonas*, and *Staphylococcus epidermidis* exists in these patients, and culture and sensitivity studies on the urine are strongly indicated (Fig. 16.1).

Most episodes of bacterial cystitis resolve spontaneously without treatment. Some episodes are produced by viruses and have no specific treatment. Despite this, most clinicians treat cases of suspected cystitis with antibiotics to speed symptom resolution and to try to avoid the spread of bacteria into the upper urinary tract. Cys-

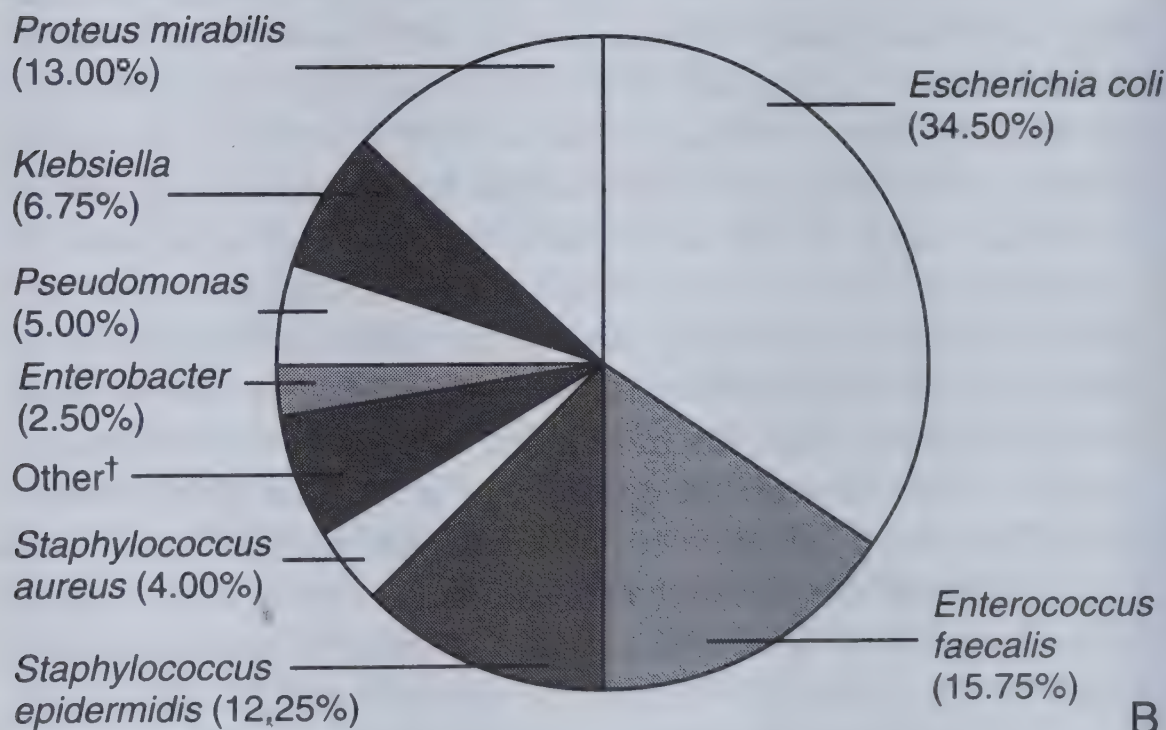
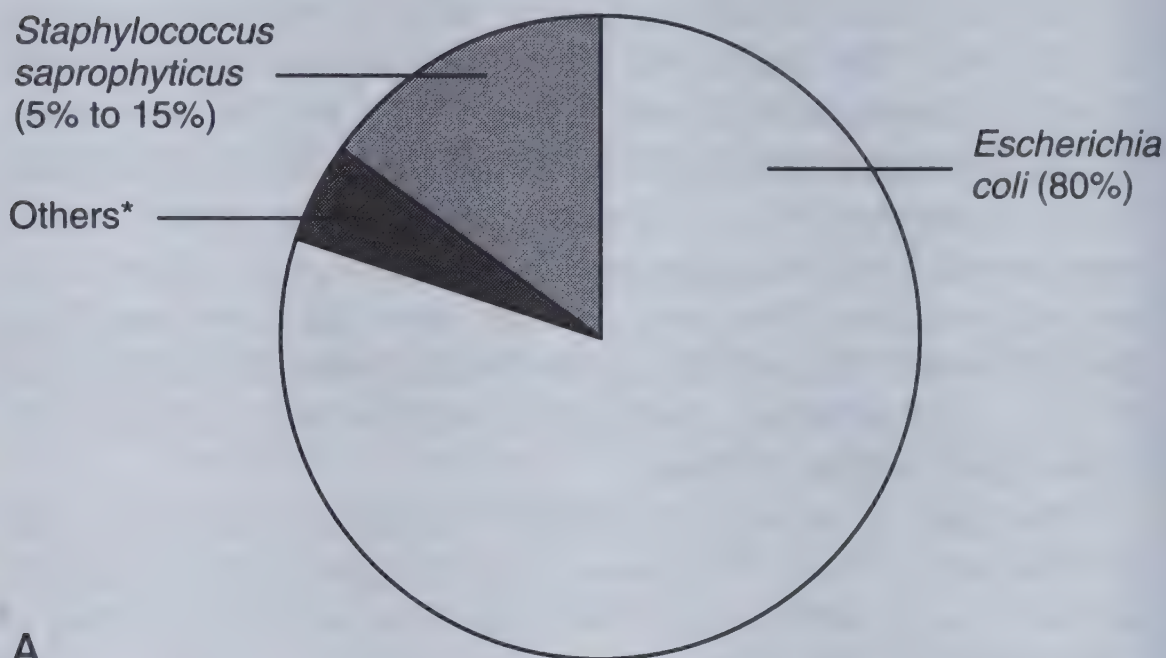


Figure 16.1. Pathogens found in uncomplicated (A)(3) and complicated (B)(11)(n = 400 inpatients with complicated or nosocomial UTI). *Occasionally isolated pathogens such as *Klebsiella* spp, *Proteus mirabilis*, and enterococci; †Other pathogens include *Serratia* (1.50%), *Acinetobacter* (1.50%), *Citrobacter* (1.00%), *Providencia* (0.25%), *Morganella morganii* (0.25%), *Candida* (0.25%), streptococci (1.50%). (Reprinted with permission from Stamm WE. Genitourinary infections in women: update on urinary tract infections and pelvic inflammatory disease. Consensus Conference Proceedings, University of Wisconsin Medical School, 1994.)

titis, if not iatrogenically acquired, is one of the easiest infections to eradicate in all of medicine. The urine concentration of the antibiotics used in its treatment tends to greatly exceed serum levels so that even organisms marginally sensitive to the chosen antibiotic will eradicate the infection. Failure of cystitis to respond to treatment should suggest the possibility of a resistant organism or a missed diagnosis (e.g., subclinical pyelonephritis or urethritis). Three- and one-day treatment courses have been tested. Three-day courses are presently preferred, as eradication occurs in about 95%, as good as a 7-day antibiotic course, with decreased cost, improved compliance, and fewer antibiotic side effects. One-day antibiotic courses are only about 65% as effective.

Since so many effective antibiotics are available, the choice of which agent to use is based upon safety (for the patient and any potential fetus or breast-feeding child), drug interaction, cost, and possible drug resistance (Table 16.1).

Hemorrhagic Cystitis

This is commonly seen and signifies bladder infection or inflammation accompanied by hematuria, gross or microscopic. About 30% of all cases of cystitis have demonstrable microscopic hematuria. Several bacterial subtypes have been shown to be responsible, and in children, adenovirus is a frequent cause. Hemorrhagic cystitis is clinically differentiated from other causes of hematuria (i.e., cancer, tuberculosis) by the presence of the “classic” symptoms of cystitis (dysuria, frequency, urgency) shortly before or concurrent with the hematuria. The hematuria resolves with treatment of the cystitis.

Recurrent Cystitis

Some women experience multiple cystitis episodes even within a year. Three episodes within a year is usually defined as recurrent cystitis. More than 90% of women with multiple UTIs have no anatomic abnormalities, and have reinfections with different bacteria, usually separated by asymptomatic intervals lasting more than 1 month (7). Any actions that might increase the risk of cystitis such as wiping back to front after defecation, or the use of diaphragms or spermicidal jellies should be altered. Voiding after intercourse should be encouraged. Combining these with acidification of the urine by taking cranberry juice may increase effectiveness further. Perimenopausal and older women should be

Table 16.1.
Antibiotic treatment for cystitis.

Drug name	Dose (adult)	Advantages	Disadvantages
Amoxicillin	500 mg tid × 3 days	Proven safety record in children and pregnancy	About 30% of <i>E. coli</i> now resistant
Trimethoprim-Sulfa	DS tab bid × 3 days	More effective and cheaper than other 3-day regimens (5) Less BCP interference	Increased risk of Kernicterus if used at end of last trimester Hemolysis if patient is G-6-PD deficient; some reports have been noted of an increase in congenital defects if taken during the 1st trimester (6)
Cephalexin	250 mg qid × 7 days	Appears safe in children and pregnancy although one surveillance report showed a small increase in birth defects (6)	About 25% of patients with penicillin allergy will be allergic to it; no tested 3-day courses.
Nitrofurantoin	50 mg qid × 7 days	Appears safe in children and pregnancy	Rare pulmonary reaction with cough, fever, SOB (usually only seen with long-term therapy); no tested 3-day courses; hemolytic anemia if G-6 PD deficient
Ciprofloxacin or Norfloxacin	250 mg bid × 3 days 400 mg bid × 3 days	Superior coverage vs. resistant pseudomonas; recommended antibiotic for outpatient treatment of complicated UTIs (with a 7-day course)	Class C agent in pregnancy; causes arthropathy in immature mammals (6) Also contraindicated in children and breast feeding

examined for the presence of uterine prolapse and cystocele, because of altered bladder neck dynamics and urine stasis associated with these conditions. The use of a pessary for uterine prolapse also, unfortunately, increases the risk of cystitis. Clinical relapse of infection (i.e., subclinical persistence), with the same bacteria after adequate treatment, is likely to be due to urinary tract abnormalities or hematogenous spread from another primary source. If this is occurring, an intravenous pyelogram is ordered to check for derangements of the kidneys or collecting system after a serum BUN, creatinine, fasting blood glucose, and HIV screen have been obtained. Renal ultrasound is substituted in those allergic to contrast dye, pregnant, or with renal failure.

If cystitis recurs despite nonpharmacological interventions, several treatment options are available. If the woman is having recurrent cystitis associated with vaginal intercourse, a single dose of an oral antibiotic after every episode of intercourse is usually effective. Single doses of nitrofurantoin 50 mg or a single-strength trimethoprim-sulfa (40/200mg) tablet or cephalexin 250 mg have all been used for this purpose. If the recurrences are not associated with intercourse, a daily dose of either single strength TMP-sulfa, or nitrofurantoin 50 mg, or cephalexin 250 mg, or pure trimethoprim 100 mg is usually effective. Patient-initiated, single-dose cystitis therapy, in which the patient has a prn prescription and initiates therapy herself when the characteristic symptoms recur, is also effective (8).

Cystitis in the Male

Cystitis in the young adult male is rare, and when it occurs is usually acquired through sexual intercourse with a woman vaginally colonized with urinary pathogens. It is more likely to occur if the man is not circumcised (9). Patients engaging in anal intercourse and patients with HIV who have CD4 counts of less than 200/cm also have an increased risk (10). Although cystitis in the male has traditionally been regarded as frequently representing a complicated infection, requiring an anatomic evaluation of the urinary tract (as outlined in the previous section), most affected patients have no such abnormalities (11). Imaging studies are best reserved for relapsing infections as in female patients. Urine cultures are indicated if cystitis is suspected in the male, and since 1- and 3-day antibiotic treatment courses have not been adequately tested in males, full 7-day treatment courses (using the antibiotics discussed in Table 16.1) should be prescribed.

Urinary Tract Infections in Children

Presentation

Whereas the older child with a UTI will present with the same symptoms as an adult patient, infants and preschool children will present with less specific symptoms such as fever, or nausea, vomiting, abdominal pain, or diarrhea. Their parents may notice an increased odor to the child's urine or the child may "fall off" his or her weight curve if chronic pyelonephritis exists..

Pathophysiology

The most common uropathogens are similar to those of adult UTIs. Uncircumcised male infants, however, are more likely to have UTIs secondary to staphylococcus aureus. Children are also more likely than adults to have abnormalities of the urinary tract in association with their infections. The most common abnormality present is vesicoureteral reflux (usually from a too short intramural segment of the distal ureter as it courses through the bladder), which allows urine to reflux back up the ureter. Reflux is found in 30% to 50% of preschool children with a UTI. Forty-five percent of asymptomatic siblings of children with reflux also demonstrate it on radionuclide cystourethrograms (12).

Diagnostic Evaluation

More accurate urine specimen collection in children can be obtained by doing a suprapubic bladder aspiration (where the growth of any bacteria is significant) or bladder catheterization (where a colony count of $>10^3$ probably represents infection). Clean-catch samples and especially bag collections are much more likely to have contaminating bacteria, and colony counts of $>10^5$ of single organisms are needed in those circumstances to be certain of infection. Contamination of clean-catch samples is less likely in boys and may still be appropriate in older girls who can comply with periurethral cleansing and who are not acutely ill.

Many children who have confirmed urinary tract infections will need radiographic evaluation for tract abnormalities, especially reflux. All boys with UTIs and girls under age 5 should have a voiding cystourethrogram or the radionuclide version to look for the presence of vesicoureteral reflux. The latter involves considerably less gonadal radiation, but is poorer in detecting certain valvu-

lar abnormalities. It is particularly important to detect this in preschool children, as the risk of damage to the renal parenchyma is greater in these children. The test should be delayed for approximately 2 weeks after treatment to avoid seeing the temporary reflux commonly present in patients with active cystitis. The natural incidence of UTIs rises as girls approach adulthood, and radiographic investigation in girls over age 5 should be reserved for those with recurrent infections or pyelonephritis. If reflux is detected, an IVP should be ordered to see if the reflux is associated with hydronephrosis or renal scarring, as their presence and severity affect therapy. If no reflux is detected, a renal ultrasound is ordered to look for congenital abnormalities in the kidneys. Most children with UTIs do not need serum measurements of their BUN and creatinine unless renal dysfunction is already suspected (hypertension, poor growth).

Treatment of Children with UTIs

Children with cystitis that is not associated with vesicoureteral reflux should be treated with a 7-day course of amoxicillin, cephalexin, or TMP-sulfa, dosed as appropriate for their weights, based on sensitivity of the organism and the patient's drug allergy history. (Note: the efficacy of 3-day treatment courses has not been proved in the pediatric population.) Children with pyelonephritis are treated for 2 weeks as are adults. Most children with vesicoureteral reflux can be treated medically, and most will have spontaneous resolution of their reflux by age 4 to 5. A strong effort should be made to avoid infection of the urinary tract as long as the reflux is present, as this combination may lead to chronic pyelonephritis, especially in preschool children. Some with chronic pyelonephritis will have early adult onset of hypertension and even renal failure (13). Smaller daily doses of amoxicillin or TMP-sulfa are usually used for this purpose, and continued until resolution of the reflux can be demonstrated usually 1 to 2 years later. Children on this prophylaxis are followed every 3 to 6 months with urine cultures obtained, even if asymptomatic. Surgical reimplantation of the distal ureter to allow a longer submucosal course where it is compressed during distention and detrusor contraction is curative in more than 90% of cases. Surgical evaluation is recommended if the child is breaking through with urinary tract infections despite antibiotic prophylaxis, if the reflux is associated with severe hydronephrosis or evidence of chronic

pyelonephritis on the IVP, or if the reflux does not spontaneously resolve.

SUBCLINICAL PYELONEPHRITIS

Some patients, with only the symptoms of cystitis, and without having any back pains, fevers or CVA tenderness, have renal parenchymal involvement with their infection. Though the organisms are the same as in uncomplicated cases, infections are more difficult to eradicate and require at least 2-week treatment courses using the same antibiotic choices as discussed. Urine culture is mandatory to identify the organism and confirm sensitivity to the chosen antibiotic.

Since symptoms are indistinguishable from cystitis, one must be alert to risk factors that promote bacterial ascension (Table 16.2). Many tests have been proposed to identify patients with subclinical pyelonephritis (antibody-coated bacterial tests, sedimentation rates), but lack of specificity has limited their clinical use. Renal cortical scintigraphy accurately shows evidence of subclinical pyelonephritis, but is rarely used clinically.

ACUTE PYELONEPHRITIS

Acute pyelonephritis is a suppurative necrosis of the renal parenchyma. It can be associated with bacteremia and even septic shock, particularly in the elderly and immunocompromised, but only rarely results in renal failure. *E. coli* produces more than 80% of the infections, but the specific bacterial subtypes tend to

Table 16.2.
Risk factors for subclinical pyelonephritis.

Symptoms for greater than 1 week before seeking treatment
Diabetes Mellitus
Immunocompromise
Pregnancy
Anatomic anomaly of genitourinary tract (duplicated ureter, cystic kidneys, etc.)
Vesicoureteral reflux
Relapse of symptoms within 3 days of treatment for cystitis
Ureteral obstruction (such as by stones or tumor)
History of acute pyelonephritis
History of urinary tract instrumentation

be fimbriated strains that can adhere to and infect the upper tract. A recurrence rate of 23% at 6 months and 40% at 4 years was noted in one study following women hospitalized for pyelonephritis (14).

Patients with acute pyelonephritis may present with an array of symptoms including back/flank pains (may be unilateral or bilateral), abdominal pains (midabdominal or epigastric), nausea, emesis, and headache. Fever is the most predictable finding (15). Elderly patients, in particular, frequently present with only the signs of sepsis.

Patients who appear septic, are hypotensive, immune-suppressed or with significant comorbid conditions (especially the elderly), are hospitalized and placed on a third-generation cephalosporin or ampicillin and an aminoglycoside intravenously, pending culture results and assuming no contraindications. The patient is switched to an oral antibiotic to complete a 2-week course when fever abates. Healthier, nonseptic patients can be treated with a 2-week course of an oral antibiotic.

BACTERIURIA

Bacteriuria is felt to be significant based on:

1. The specific counts of a single organism growth on culture.
2. The method of collection of the urine (clean catch versus catheter versus suprapubic aspiration).
3. Presence of symptoms; if a woman has symptoms of cystitis, a count of $>10^2$ coliform bacteria (per milliliter of urine) is a sensitive indicator on a clean-catch, midstream sample (10^3 in males).

Asymptomatic bacteriuria is usually not treated and therefore not screened for. Only three situations occur in which asymptomatic bacteriuria is screened for and treated:

1. Prenatal. The prevalence of bacteriuria during pregnancy is as high as 25% (if one includes *Gardnerella* and *Ureaplasma*), and 20% to 40% of pregnant females with bacteriuria develop symptomatic UTIs. This is compared with 1% to 2% incidence of symptomatic UTIs in pregnant women without bacteriuria (16). Patients who develop symptomatic UTIs, particularly pyelonephritis, have an increased rate of preterm labor and have children with lower birth weights.

Table 16.3.
Prevalence of bacteriuria in various populations

Population	Sex	
	Male	Female
Community-based		
Infants	2%	0.5%
Young Children	0.1%	1.5%
College students	<0.01%	5%
Adults (age 35–65)	0.1%	10%
Elderly (age >65)	10%	20%
Inpatient-based		
Adults	7.5%	30%
After transurethral instrumentation	20%	40%

Modified from Lipsky BA. Urinary tract infections in men. *Ann Intern Med* 1989;110: 138–150.

Urine culture is recommended for all pregnant females at about 16 weeks gestation. A 10⁵/mL colony count is considered significant if she is asymptomatic. Seven- to ten-day courses of amoxicillin, nitrofurantoin, or sulfisoxazole are used (the latter to be avoided near term because of increased risk of neonatal hyperbilirubinemia) (Table 16.1).

- 2. Children with known vesicoureteral reflux. As discussed.
- 3. Before urologic surgery. Postoperative UTIs and bacteremia are reduced by screening for and treating bacteriuria preoperatively (17).

URETHRITIS

Urethritis is the most common cause for the complaint of dysuria in the adult male. Nongonococcal urethritis is 2 to 3 times more common than gonococcal urethritis, with the ratio being even greater in higher socioeconomic groups. About 40% to 50% of nongonococcal urethritis is caused by *Chlamydia trachomatis*, and about 20% is caused by *Ureaplasma urealyticum*. Rarer causative organisms include *Mycoplasma hominis*, *Trichomonas vaginalis*, *Neisseria meningitidis*, *E. coli*, *Klebsiella*, and *Haemophilus*, as well as herpes simplex 2 virus. No organism can be isolated in about 20% of cases. Concomitant infections with gonorrhea and nongonococcal organisms are frequent.

Clinical Presentation

Urethritis can affect any age group or sex but is most commonly seen in males between the ages of 15 and 29. Patients are often asymptomatic, especially with nongonococcal urethritis, but may complain of a urethral discharge ranging from scanty and clear (more likely to be nongonococcal) to copious and purulent (more likely to be gonococcal). A burning sensation usually occurs with urination, sometimes worse with initiation. Patients often also complain of pruritus in the urethra. Urinary hesitancy, perineal, back, and testicular pains are not often seen in uncomplicated urethritis. A major concern of patients with this diagnosis may be the presumption of infidelity in their current sexual partners. This is often not a clear cut issue, as both gonococcal and nongonococcal etiologic organisms could have been present asymptotically for months or years in either partner.

On examination if urethritis is suspected but no visible discharge is present at the urethral meatus, the urethra can be milked (going from the base to the meatus) a couple of times to try to elicit any discharge. Patients are afebrile and not ill appearing. No suprapubic tenderness or scrotal swelling or tenderness is present unless the patient has developed epididymitis as a complication (about 1% of cases).

Ancillary Studies

Three basic issues must be addressed in the laboratory work-up:

1. Confirmation of the presence of urethritis (by showing >5 polymorphonuclear leukocytes [PMNs] per high-power microscopic field [hpf] in urethral secretions, or >10 to 15 wbc/hpf in the spun down sediment of the 1st 10 to 15 cc of urine voided).
2. Identification of causative organisms. Gram-negative diplococci on the gram stain of the urethral secretions or from an endourethral swab constitute presumptive evidence of *N. gonorrhoeae*. Urethritis without Gram-negative diplococci is presumed to be nongonococcal urethritis. Confirmation of these results is done by streaking an endourethral swab on Thayer-Martin medium for gonorrhea and by doing a direct fluorescent antibody test for chlamydia on a separate endourethral swab. An alternative DNA antigen polymerase

test allows detection of both chlamydia and gonococcal antigens on a single swab (18).

3. Identification of other sexually transmitted diseases that might be present in a patient with urethritis. Testing would include RPR, HIV screen and consideration of vaccination for hepatitis B.

TREATMENT OF URETHRITIS

Gonococcal urethritis is treated with Ceftriaxone 125 mg as a single intramuscular dose. Several alternative oral regimens are available, all of which are given as a single oral dose. These are cefixime 400 mg po, ciprofloxacin 500 mg po, azithromycin 1 gm po, or ofloxacin 400 mg po (some gonococcal strains from Southeast Asia and Australia have been resistant to the quinolones) (19). Quinolones and Azithromycin are not recommended in pregnancy. Patients with suspected gonococcal urethritis are also treated for presumed chlamydia as described below.

Nongonococcal urethritis is usually treated with doxycycline 100 mg po twice a day \times 7 days with erythromycin 500 mg po four times a day substituted if the patient is pregnant or allergic to tetracycline. Doxycycline must also be avoided in children. Alternative regimens include azithromycin 1 gm po \times one dose or ofloxacin 300 mg po twice a day \times 7 days (neither of these regimens are recommended in pregnancy or in children).

In patients who do not respond to a course of doxycycline, treatment with azithromycin 1 gm po \times 1 dose should be given, as a 5% to 10% of ureaplasma urealyticum are resistant to tetracyclines. An effort to isolate the more unusual causes of urethritis should be undertaken in those who do not respond to the regimens listed above. This includes a wet mount of urethral secretions for trichomonads as well as viral culture for herpes virus.

Potential Complications of Urethritis

Where urethritis exists in the male, an associated cervicitis and/or pelvic inflammatory disease is usually present in the female partner. These gynecologic infections, whether caused by gonorrhea or nongonococcal organisms, are believed to increase the risk of infertility as well as ectopic pregnancy.

Reiter's Syndrome

The classic manifestations of Reiter's syndrome are the tetrad of urethritis, conjunctivitis, arthritis and dermatitis, but cases involving parts of this tetrad are well recognized. About 1% to 2 % of cases of nongonococcal urethritis will have an associated Reiter's syndrome (20), and cases associated with gonococcal urethritis have also been reported. Besides sexually transmitted urethritis, this syndrome has also been associated with gastroenteritis secondary to *Salmonella*, *Shigella*, and *Yersinia*. Patients who are HLA-B 27 positive are more likely to develop Reiter's syndrome and usually have more severe cases with sacroiliitis. Reiter's syndrome is the most common etiology for the development of new inflammatory arthritis in a young adult. Patients presenting with these articular complaints must be questioned and examined for other components of the tetrad as well as sexual history. Some of the features in the tetrad may be absent or unnoticed by the patient. When the syndrome is seen in association with chlamydia or gonorrhea, the symptoms of urethritis usually begin 1 to 2 weeks after the sexual exposure, and the conjunctivitis/iritis, skin and mucous membrane features and arthritis typically develop within 4 weeks after the onset of the urethritis. The skin may show crusty, erythematous, hyperkeratinized lesions scattered over exposed areas, sometimes referred to as psoriaform. The tongue and soft palate may have several painless shallow ulcerations that may also occur on the penile glans. The ocular and skin manifestations usually resolve within a week. The arthritis may last up to 6 months. The joints of the lower extremity are most frequently involved, especially the knees and foot (an achilles tendonitis or plantar fasciitis is often seen). Treatment for Reiter's syndrome is supportive. Patients with urethritis are tested for chlamydia and gonorrhea and treated, although this may not hasten the resolution of the syndrome. Patients with symptomatic arthritis are given nonsteroidal antiinflammatory agents.

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Noninfectious Diseases of the Urinary Tract

Gerald D. Suchomski

Noninfectious diseases of the urinary tract make up a large, varied group of conditions. While the vast majority of these are rare, several fall into the purview of the family physician. Most the problems of the urinary tract will manifest themselves by one of three major findings: pain, hematuria, or proteinuria.

HEMATURIA

Hematuria is defined as the presence of a significant number of red blood cells (RBCs) in the urine. If there are enough RBCs to make the urine visibly bloody, the hematuria is called gross or macroscopic. Patients generally do not ignore this symptom, and readily seek medical evaluation. Most authorities cite microscopic hematuria ≥ 2 RBCs/hpf as meaningful (1).

The general rule is that any episode of gross hematuria should be evaluated. Microscopic hematuria in women warrants evaluation if infection and menstruation have been ruled out as causes. In men, hematuria due to infection should lead to evaluation for the cause of the infection.

The possibility of false-positive results from chemical testing for hematuria exists. Causes include free hemoglobin and myoglobin, peroxidase reaction interference, and other food or drug interference by discoloration of urine. The latter include berries, food coloring, ibuprofen, methyldopa, nitrofurantoin, phenytoin, rifampin, and sulfamethoxazole.

Evaluation

Table 17.1 categorizes and lists the causes of hematuria. Exercise or trauma can be provoking causes. Recent streptococcal infections would suggest glomerulonephritis or IgA nephropathy. A history of STDs or urethral catheterization would increase consideration of urethral stricture. Family history can point to hereditary causes such as adult polycystic kidney disease and Alport's syndrome (hereditary sensorineural hearing loss and progressive pyelo- or glomerulonephritis) (2). Medications associated with hematuria include anticoagulants, including aspirin, phenytoin,

Table 17.1.
Causes of hematuria.

Prerenal:

- Coagulation Defects
- Sickle cell anemia or trait
- Anticoagulant therapy

Renal:

- Pyelonephritis
- Glomerulonephritis
- Renal cell carcinoma
- Transitional cell carcinoma
- Wilm's tumor
- Trauma
- Stone
- Infarct
- Polycystic disease
- A-V malformation

Ureteral:

- Stone
- Tumor

Vesical:

- Cystitis
- Transitional cell carcinoma
- Squamous cell carcinoma

Prostatic:

- BPH
- Carcinoma
- Prostatitis

Urethral:

- Urethritis
 - Stone
 - Tumor
 - Stricture
-

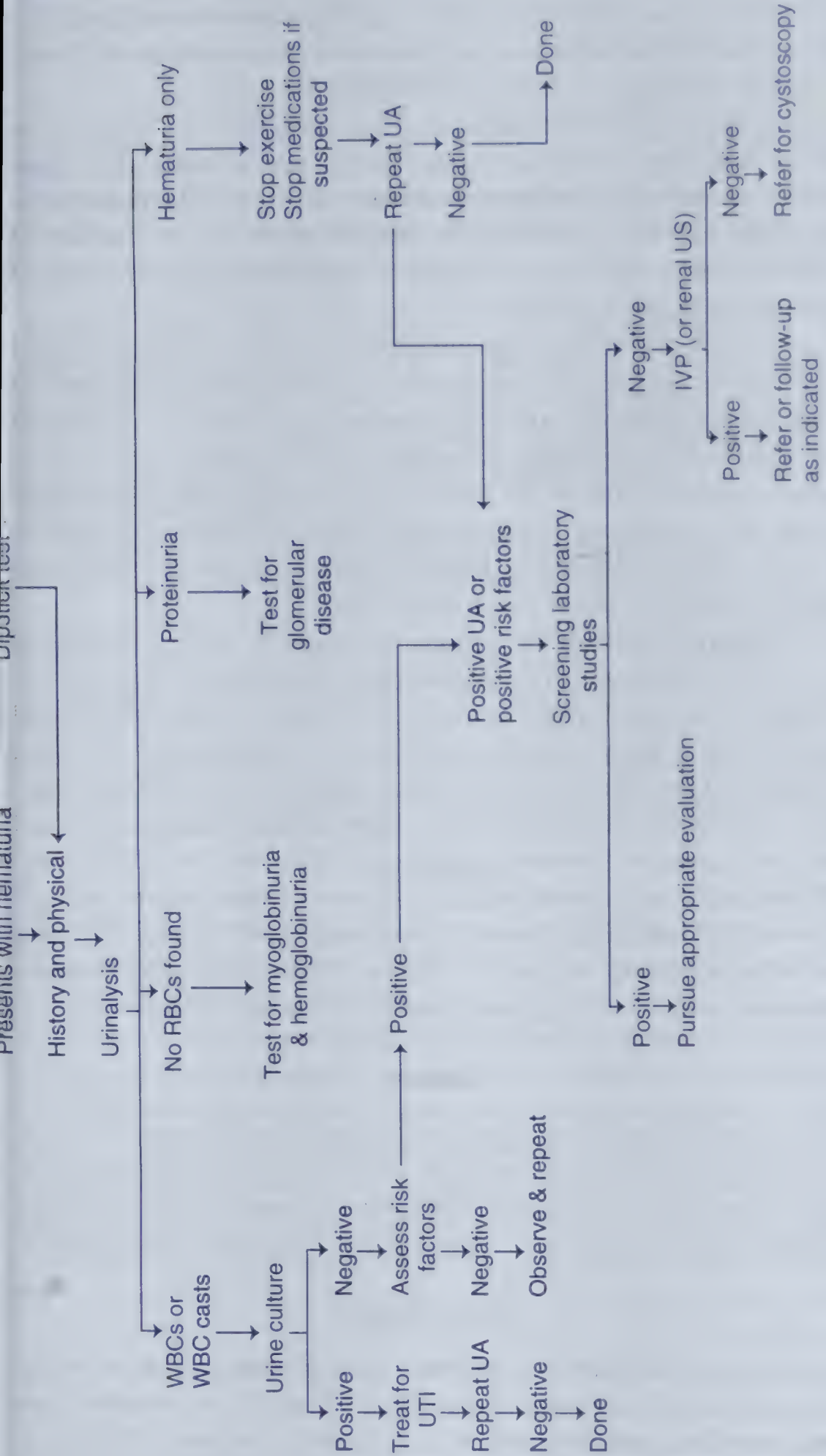


Figure 17.1. Work-up of hematuria.

rifampin, danazol, and nonsteroidal antiinflammatory agents. Occupational and social history will highlight causes of urologic tumors, such as tobacco use and exposure to a number of chemicals in the workplace that are carcinogenic.

Further evaluation should include blood test for BUN, creatinine and electrolytes to assess renal function and a CBC to assess anemia, as well as a urine culture to rule out infection. Sick cell tests, PPD, PT, and PTT should also be considered as part of the laboratory evaluation. A general algorithm for evaluation of hematuria is given in Figure 17.1.

The age of the patient is an important factor as a prioritized differential diagnosis list is developed. Evaluation of children, in particular, carries different implications, and the work-up should be tailored accordingly. Likewise, the evaluation of nursing home residents should be approached carefully, since the likelihood of underlying genitourinary abnormalities is increased. These include malignancy, bladder diverticula, silent stones, and pyelonephritis without other symptoms.

Imaging studies of the urinary tract have been the mainstay of hematuria evaluation. The intravenous pyelogram (IVP) is the traditional next test for the patient. More recently, the ultrasound scan of the urinary tract, accompanied by a plain x-ray has been considered by some to be the imaging test of choice. The advantages of IVP are its ability to show upper urinary tract transitional cell carcinoma and to serve as a rough indicator of renal function. Ultrasound is better at showing renal parenchymal lesions and can provide differentiation between solid and cystic lesions. IVP risks include radiation exposure, allergic reaction to the contrast medium, and worsening renal failure, if already present.

Causes

The causes of hematuria can be divided in many ways, but perhaps the most logical is based on anatomic location. These divisions have been discussed. Infectious causes are discussed in Chapter 16; other common diseases are discussed in this chapter.

PROTEINURIA

Proteinuria is defined as a loss of urinary protein that exceeds the average normal daily excretion of 50 to 100 mg. Most urinalyses are performed on random rather than timed complete collections. This dipstick analysis is semiquantitative, with the results graded as

Table 17.2.
Types of proteinuria.

Type	Mechanism	Example
Glomerular	Defective protein retention	Nephrotic syndrome
Hemodynamic	Increased protein filtration	Exercise
Tubular	Defective protein reabsorption	Antibiotics
Overflow	Increased protein production	Multiple myeloma

negative, trace (10 to 20 mg/dL), 1+ (30 mg/dL), 2+ 100 mg/dL), 3+ (300 mg/dL), or 4+ (1,000 mg/dL) (2). Thus, a normal random U/A should yield \leq trace (normal urinary output being 10 to 20 dL), as higher rates imply 200 to 400 mg/24 hr. Specimens with very low concentration (specific gravity <1.005) may give falsely low protein readings.

Alteration of the permeability of the glomerular basement membrane is the most common pathophysiologic mechanism for proteinuria. However, as the four basic components in the kidney (glomeruli, tubules, interstitium and blood vessels) are physiologically interdependent, multiple other mechanisms can lead to proteinuria (3). Table 17.2 characterizes proteinuria based on glomerular, hemodynamic, tubular, and overflow types. These issues are discussed in greater detail in Chapters 9 and 31.

Evaluation

The medical history, review of systems, and physical examination are essential for efficient evaluation of proteinuria, since the cause may be renal or systemic.

Microscopic examination of the urine can direct further evaluation of the proteinuric patient. The presence of erythrocyte casts indicates glomerular disease. Erythrocytes without casts are seen in glomerular disease but also occur in lesions of both the upper and lower urinary tract. If leukocytes or leukocyte casts are present, look for bacteria. Presence of bacteria indicates urinary tract infection, while absence of bacteria suggests renal interstitial disease. Fatty casts, fat bodies, or free fat are typically present in nephrosis as a result of glomerulopathy. Hyaline casts are not associated with renal disease, usually occurring after volume depletion or diuretic therapy (2).

If the microscopic examination shows isolated or low-grade proteinuria, repeat urine testing on early morning specimens

should be done. Transient proteinuria can occur with fever, congestive heart failure, exposure to cold, and strenuous exercise. Besides checking for persistent proteinuria, microscopic examination of the urine should be repeated, since urinary sediment findings may be variable (2).

Persistent proteinuria should be further evaluated by a 24-hour urine collection for protein. Normal protein in a 24-hour specimen is less than 150 mg. Microproteinuria is clinically and prognostically significant in diabetes mellitus (defined as 100 to 300 mg/24 hrs) and in hypertension (200 to 500 mg/24 hrs). Less than 1 g/24 hrs has been called "low-grade" proteinuria. Nephrosis is defined as 3.5 g/24 hrs or more and almost always reflects significant glomerular disease. Nephrology consultation is usually warranted for isolated "low-grade" proteinuria and for nephrosis.

Causes

The differential diagnosis for proteinuria is extensive due to the combination of intrinsic renal diseases, a multitude of systemic diseases, and drug effects. Table 17.3 provides a listing.

PAIN

Pain is a nonspecific symptom as it applies to the urinary tract. The easiest component is dysuria, which is usually associated with infection. Renal colic usually presents as colicky costovertebral angle or flank pain, sudden in onset and eventually radiating to the groin as the stone moves to the ureterovesicle junction. It may be accompanied by hyperesthesia of the abdominal wall, either anterior or posterior. Restlessness, vomiting, urinary frequency, and dysuria may also be seen with renal colic.

URINARY NEOPLASMS

Renal Cell Carcinoma

Eighty percent to 90 percent of renal cancers in adults are renal cell carcinomas (4). They occur most often in the sixth and seventh decades of life, with a male:female ratio of 3:1. Renal cell carcinomas arise from tubular epithelium. The risk of renal cell carcinoma is increased in smokers, with genetic factors also playing a role (3).

Table 17.3.
Differential diagnoses for proteinuria.

Primary glomerular diseases:

- IgA nephropathy
- Focal glomerular sclerosis
- Membranous glomerulonephritis
- Membranoproliferative glomerulonephritis
- Acute glomerulonephritis
- Renal vein thrombosis

Secondary glomerular diseases:

Infectious causes

Systemic diseases

- Diabetic glomerulosclerosis
- Obstructive glomerulonephritis
- Systemic lupus erythematosus
- Sickle cell disease
- Postpartum renal failure
- Preeclampsia
- Amyloidosis
- Rheumatoid arthritis

Drugs

- NSAIDs
- Captopril
- Lithium
- Probenecid
- Tolbutamide
- Heroin
- Gold

Neoplasms

- Multiple myeloma
- Leukemia
- Lymphoma

Tubular nephropathy:

Acute

- Radiologic contrast induced
- Antibiotic toxicity

Chronic

- Heavy metal toxicity
- Chronic potassium depletion

Hemodynamic proteinuria:

- Exercise proteinuria
 - Febrile proteinuria
 - Postural proteinuria
-

Hematuria eventually occurs in 90% of cases, but is usually intermittent and may be microscopic. The classic combination of costovertebral pain, palpable mass, and hematuria occur in only 10% of cases. Twenty-five percent of new cases have widespread metastases at initial diagnosis. Renal cell carcinoma metastasizes to lungs (50%), bone (33%), and to the lymph nodes, liver, adrenals and brain. Average 5-year survival is 45% (3).

Wilms' Tumor

The second most common renal cancer overall and most common in children is Wilms' tumor. It usually occurs in 2- to 5-year age groups and may be associated with aniridia, hemihypertrophy, and numerous genitourinary congenital abnormalities, plus others. At least three groups of congenital malformations have an increased risk of developing Wilms' tumor. Wilms' tumor usually presents with a large abdominal mass, but hematuria, abdominal pain, and intestinal obstruction can also be the presenting symptom.

Urothelial Carcinomas

Urothelial carcinoma of the renal pelvis is the other relatively common renal cancer. Noticeable hematuria early in the course of the disease is common, due to the location of the tumor. Survival rates depend on the grade of the tumor.

Primary neoplasms of the ureter are rare and are usually transitional cell type. Ninety-five percent of bladder tumors also arise from urothelium. They are more common in males and in industrialized areas. Several known chemical exposures increase the risk of transitional cell carcinoma, the most common of which comes from smoking cigarettes. Bladder tumors classically produce painless hematuria. Prognosis is dependent on the histologic pattern and grade and stage at initial diagnosis.

POLYCYSTIC DISEASE

Polycystic renal disease is defined as bilateral involvement of renal parenchyma with 3 or more cysts or cystic disease involving more than 25% of a single kidney (5). The term includes hereditary, developmental, and acquired disorders. The formation of cysts appears to be caused by a primary defect in tubular epithelium cell growth and differentiation (6).

The incidence of autosomal dominant polycystic renal disease is 1:1000 live births and is present in 10% of end-stage renal disease patients. Polycystic kidney disease is the most common cause of abdominal masses in newborns (7). Renal insufficiency itself seems to lead to acquired cystic changes as well.

The clinical aspects of polycystic renal disease are multiple. The most common symptoms are flank pain and hematuria. Pain is initially treated conservatively with antiinflammatory medication. Although hematuria is often the finding that leads to diagnosis of cystic diseases, it is usually secondary to conditions related to the cystic disease: trauma to the bulky cystic kidney, stones, hypertension, infection, and neoplasms (5).

The patient with polycystic disease may also develop infections, which are best treated with lipophilic antibiotics, such as trimethoprim/sulfamethoxazole and fluoroquinolones. About 20% of patients with cystic disease have renal calculi. Hypertension is a common product of progressive cystic disease. Angiotensin converting enzyme (ACE) inhibitors are effective to treat this, but have occasionally been associated with accelerated decline in renal function and therefore should be used with caution and appropriate monitoring of renal function (5).

The common belief has been that the incidence of renal cell carcinoma is markedly increased in patients with end-stage renal disease (including polycystic kidney disease patients). More recent analysis indicates that end-stage renal disease and cystic disease are coincident to the development of renal cell carcinoma, rather than causative (5).

CALCULI

Urinary calculi are a common problem in family practice settings, affecting 5% to 10% of Americans at some point. Males are more often affected, with a peak age of between 20 and 30. In addition, a familial and hereditary predisposition to stone formation has been recognized (3).

The essential factor in stone formation is an increased urinary concentration of whatever forms the stone, exceeding that component's solubility. Most stones are calcium-containing (75%). Struvite or triple stone (magnesium ammonium phosphate) make up 15%, and an additional 6% are uric acid. Cystine makes up 1% to 2% of stones (3).

Stones may be found anywhere in the urinary system, but occur most commonly in the renal calyces and pelves, followed by the bladder. Ureteral stones are most likely to get our clinical attention, however, since they are most likely to cause symptoms. Ureteral stones usually present with a characteristic pain radiating from the flank to the groin, called ureteral colic. Hematuria frequently accompanies the pain. Stones in the kidney or bladder can cause hematuria and predispose to infection, but are usually incidental findings on studies done for other reasons. The treatment options for urinary calculi have expanded tremendously over the past 20 years. Stones in the ureter can still be treated expectantly, with analgesia and fluid loading. The overwhelming majority of stones <4 mm in diameter will pass spontaneously. The patient in this situation should be monitored for signs of infection and obstruction and for failure of the stone to progress down the ureter. Failure of the stone to progress warrants a urology consultation for stent placement and definitive treatment. Some controversy exists as to two main interventions. Extracorporeal shock wave lithotripsy (ESWL) is less invasive but also less effective than endourological procedures (8).

Kidney and bladder stones generally are treated with ESWL, with a greater than 95% success rate. Complicated stone types, e.g., calyceal diverticular stones, horseshoe kidney stones and staghorn calculi require special approaches to treatment. Attempts to prevent recurrence of stones by drug treatment are not proved to be effective (9). We do know that use of the minimally invasive techniques for stone removal does not lead to higher rates of recurrence (10). Urinary calculi in children are unusual but can occur. Treatment modalities now used in adults are likewise safe and effective in the pediatric population (11).

RENAL PARENCHYMAL DISEASE

The clinical distinction between nephritis and nephrosis may be useful. Nephritis is defined as hematuria, proteinuria, renal impairment, and volume overload. It is commonly thought of as the presentation of an acute and severe renal disease, e.g., acute proliferative glomerulonephritis secondary to Group A beta-hemolytic streptococcal infection. Nephrosis or nephrotic syndrome is defined as heavy proteinuria (>3.5 g/day), hypoalbuminemia, and edema. Glomerulonephritis may present as either nephritis or nephrosis or be asymptomatic.

Nephrotic syndrome can be further divided into two major groups of disorders, primary (or idiopathic) and secondary. Primary nephrotic syndrome includes a number of entities, defined by histological and clinical characteristics. Major causes are minimal chain disease; membranous glomerulonephritis; focal segmental glomerulonephritis; membranoproliferative glomerulonephritis, and miscellaneous proliferative glomerulonephropathy. Secondary disorders are morphologically similar to primary nephrotic syndrome, but are caused by a variety of systemic illnesses, drugs, toxins, and infections. A few exceptions exist with unique histologic characteristics, notably diabetic nephropathy and amyloidosis. The primary goal of therapy in nephrotic syndrome is to treat the underlying disease. Since these conditions are often poorly or even totally unresponsive to known treatments, therapy is often directed toward the nephrotic syndrome, especially proteinuria. ACE inhibitors are the mainstay of this treatment. Dietary restriction of protein is now advocated, based on the knowledge that increased renal catabolism and blunted hepatic synthesis of albumin are major factors in the development of hypoalbuminemia, rather than the proteinuria previously thought (12). For primary nephrotic syndrome, corticosteroids and cytotoxic agents are used for immunosuppression.

Assessing the degree of renal failure is important in these diseases. This is usually done by following the glomerular filtration rate (GFR). The most precise way to do this is with an inulin or some other clearance test, neither of which is readily available. The serum creatinine value can be used, but its accuracy is impaired because the reserve capacity of the kidney must be exhausted before the creatinine actually starts to rise. A 24-hour urine collection for creatinine clearance is a better measure of renal function. A quick way to estimate the creatinine clearance is the Cockcroft-Gault formula (2):

$$C_{cr} = (140 - \text{age}) \text{ wt} / (P_{cr} \cdot 72) \text{ for men}$$

For women, multiply the result by 0.85.

C_{cr} is the creatinine clearance in mL/min.

Age is in years.

Wt is weight in kg.

P_{cr} is plasma creatinine in mg/dL.

The implications of creatinine clearance, particularly as it falls below 50 mL/minute, are discussed in the context of hypertension and of diabetes in appropriate chapters.

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Problems Unique to Females

Chapter 18

Gynecology in Primary Care

Kay A. Bauman and David R. Brown

Common primary-care problems seen related to the female reproductive tract include disorders of menstruation, pelvic infections presenting as vaginal discharge or pelvic pain, ectopic pregnancy, and disturbances of sexual function. Preventive health care includes routine screening for cervical cancer and contraceptive concerns. These topics are the focus of this chapter on primary gynecologic care for women, with the exception of contraception.

MENSTRUAL DISORDERS

Amenorrhea

Definition: No period by age 14 in the absence of growth or development of secondary sex characteristics. No period by age 16 regardless of normal growth and development with the appearance

of secondary sexual characteristics. In a woman who has been menstruating, the absence of periods for 3 of the previous cycle intervals, or a total of 6 months (1). The prevalence of amenorrhea is approximately 2% to 5% of premenopausal women.

Differential Diagnosis of Causes

Hypothalamic: Stress, weight change, eating disorders, competitive athletics, prescribed or illicit drugs, systemic illness, chronic disease, familial, lactation.

Pituitary: Idiopathic hypopituitarism, tumor, hemochromatosis, pituitary infarction (Sheehan syndrome).

Other endocrine: Hypo- or hyperthyroid, congenital adrenal hyperplasia, adrenal tumor, Addison's disease, Cushing's syndrome, diabetes.

Ovaries: Gonadal dysgenesis or agenesis, ovarian failure, polycystic ovary syndrome, tumor.

Uterus or outflow tract: Asherman's syndrome (uterine syncytiae owing to infection or aggressive curettage); pregnancy; agenesis of uterus, cervix or vagina; transverse vaginal septum; imperforate hymen; androgen insensitivity (testicular feminization).

Clinical Presentation

History: Menstrual history, growth and development, psychological or emotional stress, nutritional status, weight gain/loss, exercise and eating habits, headaches, visual disturbances, menopausal symptoms, pregnancy symptoms, acute or chronic systemic illness, hormone use, psychotropic medications, other prescription or illicit drugs, history of D&C or uterine infection; family history of genetic anomalies, autoimmune or endocrine disease, infertility, menstrual abnormalities or early menopause.

Physical examination: Tanner staging, evidence of genetic syndrome (e.g., Turner's), signs of virilization (voice, hair distribution, acne), detailed pelvic examination, thyroid palpation, galactorrhea, and pregnancy signs.

Diagnostic Considerations and Plans

1. Amenorrhea is a normal variant up to 6 months following oral contraceptives or up to 12 months following Depo-Provera, but pregnancy must still be considered (1).

2. Rule out pregnancy, and if appropriate, do pregnancy test.
3. If negative, draw thyroid stimulating hormone (TSH) and prolactin and give progestin challenge (progesterone in oil 200 mg intramuscularly once or medroxyprogesterone acetate 10 mg po daily for 5 days). If bleeding follows progesterone withdrawal, outflow tract is normal and estrogen is present, demonstrating function of ovary and pituitary axis:
 - a. With normal TSH and prolactin, and absence of galactorrhea or signs of virilization, anovulation is confirmed, and no further laboratory evaluation is necessary. Seventy-five percent of these patients will have polycystic ovaries on ultrasound, but 25% of apparently normal women will also have this finding. These women will show varying degrees of the hormonal imbalances associated with the Polycystic Ovary Syndrome, including androgen and insulin abnormalities. This, however, does little to guide therapy. For those with obesity and polycystic ovaries, weight loss is still the primary therapy for overweight PCOS patients (1).
 - b. Galactorrhea or elevated prolactin should be followed with a coned-down lateral x-ray of the sella turcica. Magnetic resonance imaging of the sella turcica is indicated if the x-ray is abnormal or the prolactin is greater than 100 ng per mL or if signs of intracranial mass are present (1).
4. If bleeding is absent or minimal:
 - a. Prescribe 1.25 mg of conjugated estrogens daily for 21 days, with 5 mg of methoxyprogesterone for the last 5 days (or use a combination oral contraceptive). Absence of flow following this regimen indicates an outflow tract problem. This may be skipped if the physical exam is normal and history does not suggest Asherman's syndrome (1) .
 - b. Draw follicle stimulating hormone (FSH) and leutinizing hormone (LH). If they are elevated, diagnose ovarian failure or menopause. Premature ovarian failure (before age 40) requires further evaluation with gynecologic consultation.
 - c. If FSH and LH are low or normal, do x-ray with coned-down view of sella turcica to rule out tumor. If coned-down view is negative, diagnose hypothalamic amenorrhea. If positive, make endocrine referral for pituitary tumor (1).

5. In the presence of signs of androgen excess, draw early morning 17-hydroxyprogesterone (17OHP), dehydroepiandrosterone (DHEAS), and serum testosterone (1, 2, 3, 4).
 - a. Normal or only mildly elevated levels of 17-OHP, testosterone, and DHEAS is the most common situation and is known as hyperandrogenic chronic anovulation or polycystic ovary syndrome (1, 2, 3, 4). Ultrasound will usually confirm the presence of polycystic ovaries, but this does little to guide therapy.
 - b. 17-OHP greater than 200 ng/dL suggests adrenal hyperplasia 21-hydroxylase variant. Do cosyntropin stimulation test and make endocrine referral (1, 3). (See Chapter 33.)
 - c. Serum testosterone greater than 200 ng/dL suggests androgen secreting tumor. Do pelvic ultrasound and make gynecology referral to look for ovarian tumor (3).
 - d. DHEAS levels of 500 to 700 micrograms/dL should be followed with cosyntropin stimulation test and endocrine referral. For DHEAS greater than 700 micrograms/dL, follow with MRI and endocrine consultation to rule out adrenal tumor (3).
6. Make appropriate referral or evaluation for the presence of Cushing's syndrome, Addison's disease, or other systemic illnesses if other stigmata of these syndromes are present.

Treatment

1. Anovulation: Consider endometrial biopsy to rule out endometrial hyperplasia or cancer if duration of anovulation is greater than 1 year. To prevent unopposed estrogen exposure to the endometrium, cycle with methoxyprogesterone acetate 10 mg daily for 10 to 14 days each month or use oral contraceptives (OCs) or Depo-Provera if contraception is required. Gynecology referral for ovulation induction may be appropriate if pregnancy is desired.
2. Hypothyroidism: Thyroid replacement should restore menses.
3. Pituitary tumor: Microadenomas are frequently followed conservatively with yearly prolactin levels and magnetic resonance imaging every 2 to 3 years. If breast tenderness or infertility is a problem, these can be managed with bromocriptine. Macroadenomas (>10 mm) are suppressed with bromocrip-

tine. Surgical debulking is also an option for either micro- or macroadenomas. Recurrence is common, however, leading to long-term cure rates of around 50%. Endocrine consultation is appropriate (1).

4. Outflow tract problems: Refer for surgical correction of anomalies. Asherman's syndrome may be treated hysteroscopically (1).
5. Ovarian failure: Prescribe hormone replacement, or OCs, since pregnancy can sometimes occur in these patients, and calcium supplementation (1500 mg daily). Premature ovarian failure is diagnosed in those under 40 years, and gynecology or rheumatology referral should be made for an autoimmune evaluation. For premature ovarian failure before age 30, do karyotype analysis. XO karyotype has implications for fertility of family members (1). XY may not be expressed as virilization in 30% of affected patients (1). Testicular tissue in the gonadal area, resulting from XY mosaicism, is high risk for malignancy and should be excised in any patient with a Y chromosome (1). Regardless of karyotype, it is recommended that all patients with premature ovarian failure have yearly pelvic examinations (1).
6. Hypothalamic amenorrhea: This is associated with decreased estrogen levels and osteoporosis. If stress, excessive exercise, or eating disorders can be identified, attempts should be made to correct them. Eating disorders require a multidisciplinary approach. Hormone replacement with low dose OCs and calcium supplementation are recommended to prevent osteoporosis (1, 5, 6).
7. Hyperandrogenic chronic anovulation or polycystic ovary syndrome: This is associated with insulin resistance and diabetes mellitus. Weight loss and/or maintenance of ideal body weight is the primary treatment and will frequently reverse the syndrome. Consider endometrial biopsy if duration of anovulation is greater than 1 year. OCs are prescribed to prevent unopposed estrogen exposure of the endometrium and to control androgen production by the ovary. Spironolactone is sometimes added if hirsutism is not controlled by OCs alone; it must be used with contraception, since the fetal effects are unknown. Hirsutism will not resolve. Gynecology referral for ovulation induction may be made if pregnancy is desired (1, 2, 4).

Dysfunctional Uterine and Vaginal Bleeding

Dysfunctional Uterine Bleeding (DUB)

DUB is endometrial bleeding of abnormal duration or amount, usually associated with anovulation, and unrelated to structural lesions or systemic illness. Most women will have some type of menstrual abnormality during their lifetime, more common in adolescent and perimenopausal years. As with amenorrhea, the abnormality may be at any level in the menstrual regulation system: hypothalamus, pituitary, adrenals, ovary, or outflow tract. Many women will pass through a period of DUB prior to the onset of amenorrhea. DUB is a diagnosis of exclusion, though in most cases, the search need not include a battery of expensive and invasive tests (1, 7). Amenorrhea and DUB share much of the same pathology: Abnormal bleeding patterns are categorized as (1): oligomenorrhea = intervals greater than 35 days; polymenorrhea = intervals less than 21 days; menorrhagia = regular, normal intervals, excessive flow and duration; metorrhagia = irregular intervals, excessive flow and duration.

Differential diagnosis: Normal, ectopic, or molar pregnancy; threatened, incomplete or spontaneous abortion; subinvolution of the postpartum uterus; retained products of conception; endometritis; intrauterine synechiae; trauma or foreign body; intrauterine device; endometrium; cervical or endometrial polyps; uterine fibroids; adenomyosis; coagulation disorders; anticoagulant therapy; renal or hepatic disease; contraceptive or other hormonal therapy; thyroid, pituitary or adrenal disease; stress, or other systemic illness (1, 7). The causes of vaginal bleeding to be considered are cancers of the cervix, vagina, vulva, or cervical erosions, or cervicitis.

Evaluation

1. Rule out pregnancy or pregnancy related disorder.
2. Characterize pattern of bleeding to determine whether it is associated with ovulatory or anovulatory cycles. The presence of regular bleeding patterns, midcycle pain, premenstrual breast tenderness or dysmenorrhea are suggestive of ovulatory cycles. If uncertain, basal body temperatures may determine if ovulation is occurring.
3. Perform the pertinent history and physical, with detailed pelvic examination. The amount of bleeding is determined

by history: number of pads used, presence of clots, and duration of flow. A hemoglobin and hematocrit will confirm anemia.

4. If anovulation is suspected, TSH and prolactin levels should be obtained (see amenorrhea).
5. If the bleeding is ovulatory (e.g., menorrhagia) or very heavy, consider evaluation for bleeding diathesis and kidney or liver failure.
6. For evident virilization, endocrine or other systemic disease should be pursued with appropriate evaluations.
7. For cervicitis, obtain cervical cultures, wet mount and potassium hydroxide (KOH) prep.
8. Endometrial biopsy is recommended by many authorities for those with prolonged anovulation (greater than 1 year) and those over 35 to 40 years to rule out endometrial cancer (1, 8, 9).
9. Transvaginal sonography, hysteroscopy, hysterosalpingography, and dilation and curettage (D&C) are reserved for those with severe, acute bleeding, failure of medical management, or physical abnormalities (1, 8).

Treatment

The goal is to end the acute episode of bleeding, prevent future episodes, and minimize long-term complications of unopposed estrogen. If pregnancy is desired in an anovulatory patient, refer for ovulation induction. Iron supplementation should be given for anemia. Failure to control bleeding with cyclic estrogen or progestational therapy is a reason for referral and/or further evaluation for uterine or systemic pathology as described previously.

Mild Bleeding.

1. Give low-dose monophasic combination OCs, starting with 1 or 2 pills twice a day for 1 week, followed by cyclic OC therapy for 3 to 6 months. If contraception is desired, OCs may be continued; if not, discontinued. Sexually active women may become unexpectedly pregnant during intermittent ovulatory cycles. OCs may be used in women over 40 years who do not have atherosclerotic risk factors.
2. An alternative progestational therapy may include any of the following: medroxyprogesterone acetate 10 to 40 mg per day initially for 5 to 10 days, then cyclically 2.5 to 10 mg daily for 10 to 14 days per month; progesterone in oil 50 to 200 mg at

4-week intervals; or depot medroxyprogesterone acetate 150 mg at 3-month intervals.

3. In the adolescent patient with mild DUB, reassurance alone may be sufficient.

Severe Bleeding. If bleeding is particularly heavy or prolonged, hospitalize patient for intravenous fluid/blood support and give conjugated estrogen 20 mg intravenously every 2 to 4 hours for 12 to 24 hours, then begin combination OCs as above. Alternate therapies include progestin IUD insertion or GnRH (gonadotropin-releasing hormone) agonist therapy in patients with systemic illness and endometrial ablation or hysterectomy if hormonal therapies have failed (10).

Dysmenorrhea

Primary dysmenorrhea is painful menstruation, cramping or laborlike, without detectable pelvic pathology. It is associated with ovulatory cycles, begins shortly after menarche, and is due to increased prostaglandin synthesis. Secondary dysmenorrhea is painful menstruation associated with identifiable pelvic pathology. More than 50% of women are seriously affected, and approximately 10% miss work or school for 1 to 3 days per month (1, 11).

Most patients also suffer from systemic symptoms, including gastrointestinal, fatigue, backache, headache, nervousness, dizziness and even syncope, some of which may be psychologically based. Symptoms begin from hours before to shortly after the onset of menstruation. The pelvic exam is normal in primary dysmenorrhea.

Secondary dysmenorrhea presents as painful menstruation in association with endometriosis (a leading cause), intrauterine device, pelvic inflammatory disease, uterine fibroids, müllerian abnormalities, adenomyosis, or other pelvic pathology. Chronic pelvic pain is not associated with the menstrual period.

Diagnosis

Primary dysmenorrhea usually has its onset shortly after menarche. Findings suggestive of secondary dysmenorrhea include abnormalities on pelvic examination, irregular or heavy menstrual flow, onset 3 or more years after menarche, infertility, use of intrauterine device, and recurrent pelvic inflammatory disease (PID). Failure of dysmenorrhea to respond to a 6-month trial of

nonsteroidal anti-inflammatory medications (NSAIDs) or OCs should prompt the search for additional pathology and gynecological referral is appropriate. Endometriosis requires laparoscopy for diagnosis. Adenomyosis should be considered in those over age 40.

Treatment

OCs generally relieve symptoms of primary dysmenorrhea. If an adequate response is not seen after several months of therapy, NSAIDs may be added for several days each month beginning at the onset of menstruation. Rarely, codeine may be required. Dysmenorrhea associated with the presence of an IUD may respond to NSAIDs as well. Therapy for other causes of secondary dysmenorrhea is directed to the individual pathology.

INFECTIONS

Candidiasis (Yeast, Monilia)

Though *Candida* may be a normal inhabitant of the vagina, lactic acid and hydrogen peroxide production by *Lactobacillus acidophilus* suppresses other microorganisms through maintenance of the vaginal pH at 3.8 to 4.2. Disturbances in the flora can allow *Candida* to proliferate and become symptomatic. These disturbances may be related to antibiotics, douching, pregnancy, poorly controlled diabetes mellitus, immunosuppression, or hormonal preparations such as in OCs and hormone replacement therapy.

Clinical Presentation

Symptoms of pruritis and thick white to yellow, curdly, adherent discharge without odor; erythematous, edematous and occasionally excoriated vagina and vulva; contiguous area of groin may also be red, weepy, and tender with satellite red macules.

Diagnosis

This is often made by clinical presentation. KOH preparation: hyphae or budding forms.

Treatment

Treatment is prescribed only if symptomatic; occasionally the male partner can also become symptomatic.

1. Vaginal preparations: all seem to have equal efficacy.

Over-the-counter:

clotrimazole	1% cream	one applicator full at bedtime for 7 days
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	100 mg supp.	one suppository at bedtime for 7 days, or one suppository twice a day for 3 days
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miconazole	2% cream	one applicator full at bedtime for 7 days
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time	100 mg supp.	one suppository at bedtime for 7 days
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Prescription:

butoconazole	2% cream	one applicator full at bedtime for 3 days
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clotrimazole	500 mg supp.	one suppository once
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miconazole	200 mg supp.	one suppository at bedtime for 3 days
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nystatin	100,000u supp.	one suppository at bedtime for 14 days
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tioconazole	6.5% ointment	one applicator full once
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terconazole	0.4% cream	one applicator full at bedtime for 7 days
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	0.8% cream	one applicator full at bedtime for 3 days
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	80 mg supp.	one suppository daily for 3 days
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2. Oral medication for refractory candidiasis:

fluconazole	150 mg	once
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ketoconazole	200 mg	twice daily for 5 days
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Both have liver toxicity as a risk and multiple drug-drug interactions.

Bacterial Vaginosis

This common vaginitis occurs generally in sexually active women but probably is not sexually transmitted. The pH and normal flora of the vagina are altered, and other bacteria such as anaerobes (*Bacteroides* sp, *Peptostreptococcus* sp, and *Mobiluncus* sp), *Gardnerella vaginalis*, and *Mycoplasma hominis* predominate. Bacterial vaginosis may be a risk factor for PID and is associated

with premature rupture of membranes, preterm delivery, chorioamnionitis, and low-birth-weight newborns. Treatment in pregnancy may decrease incidence of these sequellae. If present prior to invasive procedures such as abortion, endometrial biopsy, hysterectomy, uterine curettage, an increased rate of endometritis, PID, or cellulitis of the vaginal cuff may occur (12).

Treatment regimens are efficacious 75% to 95% of the time, but the symptoms commonly recur.

The clinical presentation includes profuse, malodorous, vaginal discharge, which is white, homogeneous, adherent; may be asymptomatic; not accompanied by vulvar or vaginal inflammation.

For diagnosis, cultures are not helpful. Three of the following four findings should be present, though many would treat empirically for fewer criteria.

1. Homogeneous white discharge.
2. Increased vaginal pH above 4.5 (not cervical pH).
3. Positive whiff test for amines with application of KOH to slide preparation.
4. On saline preparation >20% of epithelial cells are clue cells (vaginal epithelial cells that are granular or stippled with a covering of vaginal bacteria); not a predominance of leucocytes.

Treatment regimens are listed. Treatment of sexual partners is not generally helpful, but may be appropriate when the disease is recurrent. Remember to treat prior to invasive procedures.

metronidazole: (contraindicated in first trimester of pregnancy)		
	oral	500 mg 2 times a day, or 250 mg 3 times a day for 7 days, or 2 gm orally in single dose (may be slightly less effective)
	vaginal (gel)	1 applicator full (5 gm) vaginally 2 times a day for 5 days
clindamycin:	oral	300 mg 2 times a day for 7 days, or
	vaginal cream 2%	1 applicator full (5gm) vaginally daily for 7 days
		(recommended in pregnancy)
ampicillin:	oral	500 mg 2 times a day for 7 days (less effective) and less used

Chlamydia

Chlamydia trachomatis is the most common sexually transmitted infection in the United States, with more than 4 million cases per year. Most state health departments require chlamydia reporting. *C. trachomatis* is an intracellular parasite that is similar to Gram-negative bacteria, and which invades the columnar epithelial cells of the genitourinary tract. Incubation period is approximately 1 week. It can be an asymptomatic infection (70%), cause urethritis, vaginitis, or cervicitis, and can progress to acute or chronic pelvic inflammatory disease, which may result in ectopic pregnancy or infertility. The cervix tends to be the site of first infection. Risk factors are 15 to 19 years, lower socioeconomic status, multiple or new sexual partner(s). Young age (15 to 24 years) is an indication for aggressive screening of asymptomatic women. Pregnant women with active chlamydia infections place their newborns at risk for chlamydial conjunctivitis and pneumonia, premature rupture of membranes, premature birth, low birth weights, spontaneous abortion, and intrauterine death. Thus, some experts recommend screening for chlamydia in the third trimester of pregnancy. Chlamydia can also be the cause of Reiter's syndrome, and it causes 80% of the Fitz-Hugh-Curtis (perihepatitis) syndrome (13).

Clinical Presentation

Vaginal discharge, mucopurulent cervicitis, friable cervix or cervical ectopy, tender uterus with bimanual exam, spotting with intercourse, irregular menses, dysuria.

Diagnosis

To obtain specimen, clean cervix of all secretions, then insert plastic swab into endocervical canal and hold it there for 15 to 30 seconds.

1. Clinical (presumptive): mucopurulent cervicitis (MPC) with chlamydia risk factors, PID, or known coexisting gonococcal infection.
2. Culture: requires 3 to 7 days.
3. Nonculture tests: rapid, highly specific, and moderately highly sensitive, variability dependent on brand name: (a) enzyme immunoassay (EIA), (b) DNA probe, and (c) direct fluorescent antibody (DFA); requires fluorescent mono-

clonal antibody treated slide, and (d) urine screen (1st voided) by ligase chain reaction (LCR) (13).

Treatment

All regimens are for oral medications; partner is treated!

1. Tetracyclines (not in pregnancy): Doxycycline 100 mg twice daily for 7 days.
2. Fluoroquinolones (not in pregnancy): Ciprofloxacin 500 mg as a single dose, or ofloxacin 300 mg twice daily for 7 days.
3. Macrolides: Azithromycin 1 gm in a single dose (not to be taken near meals), or 500 mg erythromycin base 4 times daily for 7 days, or 800 mg erythromycin ethylsuccinate 3 times daily for 7 days.

Gonorrhea

Rates of gonorrhea (GC) in the United States have declined regularly for the last decade. The specific ages for which GC continues to increase, however, are in 10 to 19 year olds. Increasing numbers of isolates have antimicrobial resistance. Southeast Asia has particularly high rates of resistant organisms. Over time, the increase in resistant strains is expected to continuously alter recommended therapies for GC.

Highest rates of gonorrhea occur in the 20- to 24-year-old age range, closely followed by 15 to 19 year olds. GC also occurs at higher rates in inner city populations. Adolescent females have higher rates than adolescent males. African-American youth have rates many-fold higher than white and Hispanic youth. Incubation period is 2 to 7 days.

Clinical Presentation

The disease may be asymptomatic in both males and females; purulent cervical, urethral or rectal discharge; pharyngitis; salpingitis or PID (to be discussed).

Diagnosis

The clinical presentation as above is presumptive as are a sexual partner having a known GC diagnosis; culture positive; DNA probe assays; highly sensitive and specific, but may have false positives; en-

zyme immunoassay (EIA); ligase chain reaction (LCR) on first voided urine specimens.

Treatment

- Repeat positive cultures must be tested for antimicrobial sensitivity.
 - Refer sex partners for evaluation and treatment.
 - Pharyngeal infections are more difficult to eradicate.
1. Cephalosporins: 125 mg ceftriaxone IM, or 400 mg cefixime orally, or 400 mg enoxacin orally, or
 2. Fluoroquinolones: 400 mg ofloxacin orally, or (not in pregnancy) 250 mg ciprofloxacin orally
 3. Spectinomycins: trospsectinomycin 250 mg IM
 4. Penicillin/ampicillin regimens: 1000 mg ampicillin/500 mg sulbactam IM plus 1 gm probenecid orally

Hepatitis B Virus (HBV)

Hepatitis B is increasingly a sexually transmitted disease. Educational programs to reduce unprotected sexual activity have decreased infection rates among men who have sex with men, but have not affected heterosexual transmission.

Immunization of at-risk women is a reasonable way to affect rates of transmission to their partners and children. Infants who acquire HBV by perinatal transmission have historically a 90% risk of chronic infection, and 25% of these patients will die of chronic liver disease as adults. Young children who acquire hepatitis B by horizontal transmission are also at increased risk for chronic or fatal liver disease. With the availability and use of hepatitis B vaccine and immune globulin, transmission from infected mother to newborn can be greatly reduced. A woman is at increased risk by having multiple sexual partners, history of STDs, history of her own or partner's drug use, or because of ethnicity, and/or geographical location. Primary-care providers should carefully screen all women for these risks, perform hepatitis B screening (hepatitis B surface antigen and core antibody), and immunize those who remain hepatitis B negative. A caveat for the primary-care provider is when treating one STD, one must consider others, including hepatitis B.

Immigrants to the United States from China, Southeast Asia, the Pacific Basin, Africa, the Amazon Basin, and parts of the Middle East are at increased risk to carry HBV, even after the first generation of immigrants. These women can be screened at any office visit, without waiting until pregnancy for this assessment. If screened and negative, they are candidates for immunization. Pregnant women in whom no hepatitis B screening took place during their prenatal care can be screened at admission to the labor and delivery unit.

Herpes

Genital herpes infection is a common genital ulcer disease infecting more than 30 million people in the United States. It can be caused by both *Herpes simplex* I (HSV-I) and II (HSV-II), but HSV-II predominates (70% to 90%). Most HSV infections are asymptomatic. Initial infection occurs through mucosal surfaces. Subsequently virus particles are transported along peripheral nerves to the dorsal root ganglia, where they remain latent and can cause exacerbations of disease.

Clinical Presentation

Primary herpes is a more extensive and longer lasting infection than recurrent herpes and is often preceded or accompanied by symptoms of fever, malaise, headache, and/or paresthesias. Lesions can be on the perineum, vulva, vagina, or cervix, and with initial infection can be accompanied by tender inguinal adenopathy. Two crops of vesicles may occur. Healing usually occurs by 3 weeks.

In one study of 457 active herpes patients, 89% experienced a recurrence during approximately 1 year of follow-up. The average recurrence was once every 3 months, and 20% had greater than 10 occurrences in the first year. Women had somewhat fewer recurrences than men (14). Often a prodrome of tingling or itching occurs prior to recurrent eruption of vesicles. Shedding of virus lasts for 2 days, but vesicles can take 1 to 2 weeks to heal.

Diagnosis

Clinical recognition accompanied by a characteristic history is often sufficient to diagnose herpes. Viral culture remains the gold standard. It is most likely to be positive in the first few days of the vesicles, but it can be falsely negative 20% to 30% of the time.

Viral culture takes approximately 5 days. Newer tests such as enzyme-linked immunoassays for viral antigen still have too low a sensitivity to be clinically useful. The Tzanck test is specific but not sensitive.

Treatment

The oral antiviral medications, acyclovir and the newer famciclovir, are the drugs of choice. Treatment must be started early in the clinical presentation when virus is replicating. Therapy reduces viral shedding and shortens time to healing, especially in primary herpes. For herpes that is severely recurrent, suppressive therapy can reduce recurrences by 80%.

Medications:

Primary herpes:	acyclovir 200 mg 5 times a day for 10 days, or famciclovir 125 mg twice a day for 10 days
Recurrent herpes:	acyclovir 200 mg 5 times a day for 5 days, or famciclovir 125 mg twice a day for 5 days
Suppressive:	acyclovir 200 mg twice a day (or up to 5 times a day)

Drug resistance to acyclovir has been detected, particularly in patients coinfecting with human immunodeficiency virus (HIV). In these patients, foscarnet can be used.

Vaccine trials are ongoing, both for a primary vaccine for people not infected and for an immune-boosting vaccine for people already infected.

This disease has a particularly high psychosocial toll because of its chronicity, viral shedding and thus infectivity even when no lesions are present, and potential for transmission not only to partners but also to newborns. Physicians must counsel and support patients through the emotional turmoil that can accompany genital herpes.

Human Immunodeficiency Virus (HIV) Disease

In 1994, 41% of women with AIDS reported infection by intravenous drug usage (IDU), 38% by heterosexual contact, and 2% by receipt of contaminated blood or blood products (15, 16). After injection drug use, increased number of sexual partners, increased frequency of vaginal or anal intercourse, and a decreased use of condoms put women at greatest risk for HIV transmission.

As primary health care providers increasingly understand that sexual transmission is an important risk for women, they are more likely to include HIV screening in STD evaluations.

Improved risk taking history will undoubtedly help physicians identify more women who are HIV positive. That screening can include geographical location, race or ethnicity, economic status, numbers of sexual partners, sexual behaviors, history of injection drug use, history of sex while high on drugs, history of exchanging sex for drugs, history of transfusion, diagnosis of tuberculosis, type and frequency of contraceptive method used, and drug and sexual behaviors of the primary sexual partner. Nonetheless, this whole series of questions will fail to identify many women who are HIV positive.

Gynecologic Presentation

Caring for women with HIV differs little from caring for men except in the areas of gynecological care and pregnancy (see Chapter 29). Recurrent or refractory vaginal candidiasis can be the presenting complaint, and it can occur even before oral thrush. Oral antifungal agents, such as ketaconazole or fluconazole, may be required. Immune suppressed women also have increased evidence of cervical HPV (human papilloma virus) infections and an increased progression to carcinoma in situ and invasive cancer. Current recommendations for Pap smear screening for asymptomatic women is 2 tests 6 months apart. If these tests are negative, annual testing is adequate. Some providers recommend more frequent Pap tests once the CD₄ count drops below 500, such as every 6 months, or even every 3 months once the CD₄ count drops very low. Although colposcopy is recommended for the evaluation of any abnormal Pap test, some physicians recommend routine colposcopy for all HIV-infected women.

Screening routinely for other STDs in HIV-infected women is important. Often HIV will coexist with ulcerative disease, such as herpes simplex and syphilis, but also with nonulcerative disease, such as chlamydia, gonorrhea, and trichomonas.

Pelvic inflammatory disease (PID) has a more complicated course, with more frequent severe pain, fever, cervical inflammation, and discharge. Women with AIDS more commonly need inpatient treatment, but nonetheless, seem to respond to standard treatments.

Fertility counseling needs to be made available for HIV-infected women and may include both a hormonal method of contraception and condom use. Nonetheless, as more women are infected with HIV, more pregnant women will be infected. The current U.S. rate is approximately 1.6 infected women per 1,000 giving birth. This varies widely by geography, race, and ethnicity and urban versus rural location. Fertility does not seem to be affected by HIV infection, nor does the progress of HIV disease affect pregnancy. Transmission from mother to newborn has generally been in the range of 13% to 30%, but a recent well-designed study showed that zidovudine (ZDV) could decrease transmission during pregnancy from 25.5% to 8.3% (17).

In this clinical trial, zidovudine was given after 14 weeks of gestation at a dose of 500 mg daily and during labor at a 2 mg/kg loading dose and then 1 mg/kg per hour infusion. The newborn was given ZDV at a dose of 2 mg/kg every 6 hours for the first 6 weeks. Thus, primary-care physicians should offer HIV testing to pregnant women. Women who test positive must be encouraged to take ZDV to decrease the risk of HIV transmission to their infants.

Rates of transmission to newborns by breast feeding vary from 16% to 87% (18). Thus, HIV-positive mothers should be advised against breast feeding.

Syphilis

The United States experienced an increase in syphilis cases in the second half of the 1980s, reaching a peak of 20.3 per 100,000 population in 1990. The cases have once again declined (to 8.1 by 1994), but mini-epidemics continue to occur. Major contributors to this epidemic have been the increase in crack cocaine use and the exchange of sex for drugs.

Syphilis is caused by *Treponema pallidum*, a spirochete that is generally transmitted sexually but can be transmitted congenitally from mother to newborn. The incubation period for sexual transmission is typically 3 weeks after sexual contact.

Clinical Presentation

The initial lesion is usually a single painless indurated ulcer (chancre), usually on the genitalia, at the site of inoculation and accompanied a few days later by regional, painless adenopathy.

Half of untreated patients progress to secondary syphilis about 2 months after the chancre has healed. This stage is characterized by a maculopapular, generalized rash that includes the palms and soles. The rash resembles pityriasis rosea without the herald patch. Additional lesions associated with secondary syphilis are condyloma lata, which are lobular papules of the vulva or perianal area. The remaining half of untreated cases progress to the latent phase.

Tertiary syphilis can occur 5 to 10 years after infection and involves mucocutaneous nodules and gummas, cardiovascular lesions (e.g., aortitis) and CNS involvement.

Diagnosis

1. Darkfield microscopy: darkfield identification of spirochetes in serous exudate from suspicious lesion, the only method of diagnosis in the primary stage.
2. Nontreponemal tests: VDRL (Venereal Disease Research Laboratory) and RPR (Rapid Plasma Reagin), equally sensitive and excellent for screening; can be qualitative or quantitative titers; become positive 3 to 4 weeks after exposure and usually revert to negative after treatment of primary or secondary syphilis (in 1 to 2 years).
3. Treponemal tests: FTA-ABS (fluorescent treponemal antibody absorption), and MHA-TP (microhemagglutination *T. pallidum* assay) are confirmatory tests and not used quantitatively.

Treatment

1. Primary, secondary, early latent, and exposed patients: penicillin G benzathine, 2.4 million units IM, single dose.
2. Late latent (>1 year) or unknown duration: penicillin G benzathine, 2.4 million units IM once weekly for 3 weeks.

Penicillin-allergic patients preferably can be desensitized to penicillin or treated with oral doxycycline 100 mg twice daily for 2 weeks.

Trichomonas

This flagellated protozoan causes about 25% of vaginal infections, although many women with the infection are asymptomatic.

Clinical Presentation

It presents as a yellow to green frothy vaginal discharge with a fishy odor, occasionally accompanied by mild itching; inflamed vagina; cervix inflamed, friable and at times with petechiae, called a “strawberry cervix”; may coexist with other STDs.

Diagnosis

Diagnosis is based on vaginal pH > 4.5; wet mount/saline preparation, distinctive flagellated, motile organisms, with an abundance of WBCs; can be diagnosed on Pap tests; acridine orange stain of dried slide can enhance accuracy of diagnosis.

Treatment

Also treat sexual partners!

oral metronidazole: 2 gm in single dose, or
250 mg 3 times a day or 500 mg twice a
day for 1 week
(avoid in first trimester of pregnancy)

Venereal Warts (Condyloma Acuminata)

Human papillomavirus (HPV), a DNA virus, is a widespread, sexually transmitted infection that not only causes venereal warts, but can increase the risk of cervical dysplasia and cancer, discussed later in this chapter. Polymerase chain reaction tests (PCR) indicate that in some high-risk populations, as many as 30% to 40% of sexually active women carry HPV on the cervix. Most have never had a history of venereal warts. Partners of infected people have a rate of 60% to 90% HPV infection, usually within about 3 months of sexual contact. Risk factors include multiple sexual partners, early age of first sexual intercourse, history of other STDs, smoking and young age. Pregnancy can accelerate growth. Many lesions regress spontaneously.

Clinical Presentation

Skin-colored growths from a few millimeters to several centimeters in diameter, usually asymptomatic, but can cause itching, pain, burning or bleeding; can occur on cervix, vagina, introitus, urethra,

labia, perineum, and perianal areas; HPV can present with cervical intraepithelial neoplasia, carcinoma in situ or invasive cancer.

Diagnosis

Usually by clinical presentation or abnormality on Pap test; application of 5% acetic acid to better define infected areas allows for more thorough treatment, but not eradication. PCR test and a DNA hybridization probe are not yet recommended for widespread use.

Treatment

No single treatment modality is superior to any other, and all modalities are followed by high recurrence rates:

Chemical/caustic agents: podophyllin (10% to 25%) in compound tincture of benzoin (weekly applications by physician); 5 fluorouracil; weekly applications of trichloroacetic acid (80% to 90%); newly available by prescription is podophyllotoxin cream 0.5%, for home management by patients (apply twice daily for 3 days per week for 4 cycles).

Surgical ablation: cryosurgery (liquid nitrogen), CO₂ laser therapy, electrocoagulation, loop electrosurgical excision procedure (LEEP), surgical excision.

Interferon: intralesional injection, intramuscular or subcutaneous.

Pelvic Inflammatory Disease (PID)

Infections of the upper genital tract can be asymptomatic, limited to endometritis, or more extensive with salpingitis or pelvic peritonitis; can be acute or chronic; can be mild, allowing outpatient management, or severe, requiring inpatient management. PID generally occurs after sexual activity begins, and risk factors include multiple partners, history of STDs, and a previous episode of PID. It is a common sequella to both gonorrhea and chlamydia infections. Short-term complications include tubo-ovarian abscess and perihepatitis (Fitz-Hugh-Curtis syndrome); long-term include chronic pelvic pain, ectopic pregnancy, and tubal infertility. PID is usually polymicrobial: *Neisseria* gonorrhea and *Chlamydia trachomatis*, anaerobes such as *Bacteroides* sp, *Peptostreptococcus* sp, *Prevotella* sp, *Mycoplasma ho-*

minis, *Ureaplasma urealyticum* and *Mycoplasma genitalium*, and facultative bacteria including *Gardnerella vaginalis*, *Streptococcus* sp, and coliforms. Prevention of PID is important to consider; it may be effected by screening for Chlamydia and GC prior to an elective abortion and treating all positives (19).

Clinical Presentation

PID presents as lower abdominal or adnexal tenderness; tenderness on motion of the cervix; fever; palpation of a mass by bimanual examination or noted on ultrasound. Most patients have mild PID and are without fever, leucocytosis, or vaginal discharge. No finding is pathognomonic for all cases.

Diagnosis

Clinical findings are most helpful in diagnosis; culture for gonorrhea and Chlamydia; elevated erythrocyte sedimentation rate or C-reactive protein can support the diagnosis.

Treatment

Male sexual partners of women with PID have a high carrier rate for both Chlamydia and gonorrhea, two-thirds of which may be asymptomatic (20). If an IUD is present, it must be removed. Broad spectrum treatment is necessary, usually aimed at Chlamydia and gonorrhea (PPNG), and the anaerobes and mixed aerobes that can cause infection. No data are available showing fertility to define "cure," rather than relief of symptoms or microbiological cure.

Selected regimens: oral antibiotics are taken for 10 to 14 days.

Outpatient: cefoxitin	2 gm IM, 1 gm probenecid plus doxycycline 100 mg twice a day
ceftriaxone	250 mg IM (ceftizoxime or cefotaxime can be substituted) plus doxycycline 100 mg twice a day
ofloxacin	400 mg orally twice per day plus metronidazole 500 mg twice a day
ofloxacin	400 mg orally twice per day plus clindamycin 450 mg 4 times a day

amoxicillin/ clavulanic acid:	1.5 gm four times a day plus doxycycline 100 mg twice a day
azithromycin	2 gm orally plus metronidazole 500 mg twice a day
azithromycin	2 gm orally plus clindamycin 450 mg 4 times a day

Hospitalize if pregnant, if abscess is present, overt peritonitis, or cannot tolerate or fails to respond to outpatient management.

ECTOPIC PREGNANCY

Most commonly this occurs in the ampullary region of the fallopian tube (80%), but may occur at other parts of the tube (18%), within the ovary (0.2%), abdominal cavity (1.4%) or within the cornua (1%) or cervix (0.2%) of the uterus (1). It "is the leading cause of pregnancy-related death during the first trimester, accounting for 9% of all pregnancy-related maternal deaths (in 1992)" (21). Heightened suspicion for ectopic pregnancy is the cornerstone of early diagnosis, which now leads to intervention prior to fallopian tube rupture in the vast majority of cases. Incidence rates have been increasing, partly because of advances in the treatment of infertility (1). Currently, approximately 2% of all pregnancies are ectopic (21). Fatality rates have declined 90% since 1970, as advances in ultrasound, sensitive assays of the beta subunit of human chorionic gonadotrophin (β -hCG) and laparoscopy have led to earlier diagnosis and treatment. Approximately half of all cases of ectopic pregnancy are now treated on an outpatient basis (21). Surgical therapy via the laparoscope with a tube-sparing procedure (salpingostomy) is considered the current gold standard of therapy, though medical management with methotrexate is increasingly advocated as a safer and much cheaper alternative to the surgical approach in selected early ectopic pregnancies (1, 22, 23).

Clinical Presentation

The classical presentation, now uncommonly seen, is delayed menses, vaginal spotting and abdominal pain, with or without an associated adnexal mass, progressing to shock due to tubal rupture

and associated hemorrhage, occurring most commonly from 6 to 12 weeks after the last menstrual period (LMP). Early in the course, ectopic pregnancies may be entirely asymptomatic or present with any amount of abdominal or pelvic pain or vaginal bleeding. *Early detection requires heightened suspicion in any patient with delayed menses.*

Diagnosis

1. Any patient with a delayed menstrual period and vaginal spotting or abdominal pain should be evaluated with a qualitative pregnancy test; if positive, should be further evaluated with ultrasound.
2. The presence of an intrauterine gestational sac with a yolk sac and/or cardiac activity effectively rules out an ectopic, since coexisting intrauterine and ectopic (heterotopic) pregnancies are very rare. Special caution is required in patients undergoing assisted reproduction, in whom the rate of heterotopic pregnancies is 1:100 (1, 23). A pseudogestational sac, due to blood or exaggerated decidual reaction within the endometrium, may be present in up to 10% of ectopic pregnancies. Pseudosacs may be differentiated from normal gestational sacs by the absence of a yolk sac, oval or oblong shape, irregular margins, and presence within the endometrial cavity rather than the decidua. The presence of a complex adnexal mass and free fluid in the cul-de-sac strongly suggests an ectopic pregnancy. Free fluid by itself is suspicious for intraabdominal bleeding, particularly if it is echogenic. If fetal cardiac activity is seen within the adnexal mass, it confirms ectopic pregnancy. The place of doppler imaging to better define the blood flow to an adnexal mass or early intrauterine sac is still being defined (1).
3. If the ultrasound fails to identify an intrauterine or ectopic pregnancy, a quantitative β -hCG measurement should be obtained. β -hCG levels double approximately every 2 days until above 10,000 mIU/mL International Reference Preparation (IRP) (1). The zone of discrimination, the level of β -hCG above which an intrauterine gestation should always be visible by transvaginal sonography, is 1000 to 2000 mIU/mL (IRP) (1, 21), depending on the operator and equipment. β -hCG levels below the discriminatory zone should be repeated in 48 hours. A rise of less than 66% in 48

hours suggests an abnormal gestation, possibly ectopic (23). Once β -hCG levels rise above the zone of discrimination, ultrasound should be repeated. *Failure to identify an intrauterine pregnancy when β -hCG levels are above the zone of discrimination is an ectopic pregnancy until proved otherwise.*

4. Progesterone levels above 25 ng/ml are associated with normal gestations 98% of the time (1). Levels below 5 ng/ml are invariably associated with nonviable pregnancies, either intrauterine or ectopic. Levels of 5 to 25 are indeterminate, but 81% of ectopics will have levels below 15ng/mL (23).
5. Culdocentesis may influence a surgical decision in the case of a hemodynamically unstable patient when ultrasound is unavailable.

Treatment:

Once the diagnosis is made or if it is being strongly considered, gynecologic consultation should be obtained. As medical management becomes more common, consultation may not be necessary for all cases.

1. In hemodynamically stable patients without significant bleeding or evidence of tubal rupture, who have small ectopic pregnancies (<3 cm) and declining β -hCG levels, expectant management may be considered. This entails following symptoms, serial ultrasounds and β -hCG levels.
2. Management options include:
 - a. If levels plateau but do not fall, intervention is necessary.
 - b. Uterine curettage may be useful to distinguish between ectopic pregnancy and incomplete or threatened abortion.
 - c. Diagnostic laparoscopy.
 - d. Medical treatment with methotrexate: single- and multiple-dose intramuscular methotrexate regimens have both had promising results. Contraindications for methotrexate therapy include hepatic, renal, peptic ulcer or hematologic disease, hematologic instability, the presence of fetal heart tones, a large ectopic, or a coexisting IUD. Careful follow-up is important (22, 23, 24).
3. In the absence of an intrauterine gestational sac, with a β -hCG level above the zone of discrimination, management is controversial. A gynecologist would be involved in decision for treatment options.

4. If the patient has a large ectopic (>3 to 4 cm), the presence of fetal cardiac activity within an ectopic, or hemodynamic instability, surgical therapy is indicated (1): salpingostomy or salpingectomy, depending on future fertility, desirability and prospects.
5. Rhogam is indicated for Rh-negative mothers with ectopic pregnancies beyond 8 weeks gestation.

Follow-up

Regardless of treatment option, β -hCG levels should be followed until they are nondetectable, around 4 weeks in the average case, but possibly as long as 4 months.

CERVICAL CYTOLOGY: THE PAPANICOLAOU (PAP) SMEAR

The lifetime risk of dying of cervical cancer in the United States is 0.3% (25). Five-year survival is about 90% for localized disease and 14% for advanced disease. Since it has been instituted widely, Pap smear screening is credited with a 70% reduction in the incidence of invasive cervical cancer and cervical cancer mortality (26). Human papillomavirus (HPV) is now felt to be the causative agent in cervical cancer and is transmitted through sexual activity. A spectrum of disease is seen in association with the presence of HPV DNA from simple condyloma with or without mild dysplasia through invasive carcinoma. Condyloma and mild dysplasia frequently regress without treatment. No current modalities are able to differentiate those abnormalities that will regress from those that will progress to more severe dysplasia or invasive carcinoma. HPV DNA testing and typing is not yet of clinical usefulness.

Frequency and Duration of Testing

Pap testing is performed on all women who are or have been sexually active and who have a cervix. If the sexual history is unreliable, testing should begin at age 18 years. Some experts recommend 3 annual negative smears before proceeding to a 3-year interval. A history of abnormal smears requires testing more frequently. Once a woman reaches age 65 with consistently normal smears, testing may be discontinued. Elderly patients with no reliable history of normal smears need continued testing. Those who have had a hysterectomy for reasons other than cervical cancer do not benefit from further Pap testing. Office systems for patient call-

back increase the compliance rate for Paps. Failure to follow up abnormal smears is an important cause of delayed treatment.

Interpretation and Follow-up

Most authorities recommend using the Bethesda System for reporting of cervical cytology results (27). These reports contain a statement of the adequacy of the specimen and a descriptive diagnosis (26). Smears reported as “adequate, but limited by” may or may not be repeated depending on the clinical suspicion (28). The absence of endocervical cells by itself does not mandate repeating the smear sooner than usual (28).

Benign or Reactive Cellular Changes

Mild inflammation may be followed with annual smears. Moderate or severe inflammation should prompt an evaluation for causes of cervicitis, and treatment if an etiology is identified. Repeat testing in 6 months, then annually, if the smear reverts to normal. Pap smear diagnosis of trichomonas or chlamydia should be corroborated by the appropriate diagnostic test. If tests are negative, treatment need not be initiated, and follow-up smears can be repeated annually. Abnormalities that persist should be evaluated by colposcopy.

Epithelial Cell Abnormalities

Atypical Squamous Cells of Undetermined Significance (ASCUS). Defined as either reactive or premalignant/malignant process. If the report favors inflammation, follow as with moderate inflammation above. If the report favors dysplasia (premalignant/malignant), then proceed as with low-grade squamous intraepithelial lesion (LGSIL). If follow-up is uncertain or there is a previous history of squamous intraepithelial lesion (SIL), proceed directly to colposcopy. In the postmenopausal woman, treat with 4 weeks of estrogen cream, repeat smear, and if normal, follow up annually, and if abnormal, proceed to colposcopy (28, 29).

Low-Grade Squamous Intraepithelial Lesion (LGSIL). LGSIL includes the older categories of HPV, mild dysplasia and CIN 1. LGSIL may be followed with repeat Pap testing every 6 months for 2 years, then annually. If any abnormality is found on repeat testing, proceed to colposcopy. Alternatively, colposcopy may be

performed after only one LGSIL smear, especially if follow-up is uncertain (28, 29).

High-Grade Squamous Intraepithelial Lesion (HGSIL) or Squamous Cell Carcinoma. HGSIL includes the older categories of moderate or severe dysplasia, CIN 2 or 3, and carcinoma in situ (CIS). With either HGSIL or squamous cell carcinoma, evaluate with colposcopy and directed biopsies (27), and gynecologic referral as indicated.

Atypical Glandular Cells of Undetermined Significance (AGUS). AGUS should be subclassified as favoring a benign reactive or neoplastic process. If neoplasm is favored, referral should be made for colposcopy, endocervical curettage, and possible cone biopsy to rule out adenocarcinoma. Management of AGUS that is unqualified or that is reported as favoring a benign process has not been clearly established. The evaluation may include colposcopy with endocervical curettage (ECC) or hysteroscopy. AGUS felt to be of endometrial origin should be referred for ECC with fractional dilation and curettage or hysteroscopy (27, 28).

SEXUAL DYSFUNCTION

Sexual History Taking

Sexual history taking legitimizes sexual topics as “OK” for the family physician’s office. Two simple questions: (a) “Are you sexually active?” and, if yes, (b) “Do you have any sexual difficulties or concerns?” can open the door to discussing a range of sexual topics such as function, pregnancy planning and prevention, STDs, sexual abuse, or sexual satisfaction. The challenge to the physician is to determine if the cause of sexual dysfunction is a communication problem with the partner, a secondary effect of a medication or medical illness, a psychiatric problem, or a true problem of sexual function. Education and information may be all that is needed to reassure the patient that her concerns fall in the framework of normal sexual function.

Specific Types of Sexual Dysfunction or Disorders

Desire phase: Decreased libido is the most common sexual complaint reported to generalist physicians. Testosterone is the most significant hormone governing desire in both men and women.

Thus a surgical cause of decreased libido may be oophorectomy (Chapter 19). Medical conditions associated with decreased desire may be depression or its treatment, alcoholism or cirrhosis of the liver, or use of antihypertensive medications. Nonorganic causes of decreased desire are more common and are often the repression of sexual drive secondary to fatigue, stress, poor self-esteem, conflict in the relationship or loss of attractiveness to one's partner. More complex psychiatric conditions for decreased libido are previous traumatic sexual experiences, phobias toward sex, and fear of intimacy; these usually require referral to a skilled therapist.

Arousal phase: Psychogenic causes for arousal problems may be sexual orientation conflicts or a history of abuse. Age is relevant: organic causes are unusual prior to age 40. Acute versus chronic onset is also relevant: chronic is more likely organic. Decreased estrogen levels causing thinning of the vaginal mucosa may occur with surgical or natural menopause, and these conditions may require increased stimulation, artificial lubrication and hormonal therapy for the arousal phase to occur. Treatment of arousal phase problems includes sensate focus exercises, a diversion from performance requirements and refocusing on pleasuring, and emphasis on sexual communication with permission to take turns being the center of attention in a given sexual encounter.

Orgasmic phase: This dysfunction in women is less often secondary to a medical condition and more often requires education and reassurance as major foci for its resolution. The woman's upbringing may not have given her permission for self-exploration such as masturbation, and thus she may need to learn the type of stimulation needed to achieve orgasm and that, for most women, it does not come with only penile thrusting.

Dyspareunia can be primary or secondary, complete or situational, and can result from the infections already addressed, irritation such as to a contraceptive lubricant or bath oil, lack of vaginal lubrication, endometriosis, or a tight hymeneal ring. It can also be psychogenic pain from previous abuse or trauma. Most often the etiology can be determined by a careful history and pelvic examination and be treated by the family physician.

Vaginismus is a treatable condition of involuntary tightening of the pubococcygeal muscles that prohibits penile penetration. These women also may have difficulty with a speculum or bimanual examination. Possible etiologies are previous sexual

trauma, painful pelvic examination or strict religious upbringing. Teaching the woman to keep the pelvic floor muscles relaxed through progressive exercises, usually first with her own fingers, then her partner's fingers, then gentle admission of the penis, and then her control of the thrusting (superior position).

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Problems of the Female Climacteric

David R. Rudy

NATURAL MENOPAUSE

The physiological definition is permanent cessation of menses due to ovarian failure in the face of elevated follicle stimulating hormone (FSH) after age 40. Clinical definitions include typical symptoms in the appropriate age setting such as vasomotor and emotional symptoms and/or cessation of menstrual periods, even for only a few months, with the corroborating finding of elevated FSH level >40 mIU/mL (>40 IU/L), 20 mIU by newer sensitive testing; 1 year without menses in the appropriate clinical setting; FSH level >40 mIU/mL in an atypical setting, even if menses resume temporarily. Amenorrhea alone, existing for less than 6 months, requires confirmation by FSH. If FSH is measured with newly increased sensitivity, some physicians feel the cut point should be lowered to 20 mIU/mL. The rapid fall in estrogen results in thinning and drying of vaginal and other mucosae, dysuria and dyspareunia; elevation of total and depression of high density lipoprotein cholesterol; increased protein catabolic effects on the osteoid matrix of cancellous bone; reduced production of 1, 25 dihydroxycholecalciferol (vitamin D³) from hydroxycholecalciferol, which results in intestinal malabsorption of calcium, and loss of estrogen's parathormone inhibiting effect.

Clinical Manifestations of Acute Natural Menopause

Amenorrhea may set on suddenly but is usually heralded by irregular periods for several months, and as long as 1 year. Along with previously mentioned changes, vasomotor instability produces hot flashes in about 70% of women in attacks lasting 5 to 10 minutes, reversible with conjugated equine estrogens (CEE, Premarin) 0.3 mg daily. The relative excess of androgens from the ovaries, intact except for estrogen production, allows continuation of the libido and often results in an increase in facial hair. Psychological sequelae of menopause include lability, anxiety, depression, and rapid mood changes. Confusion and memory loss may occur. Insomnia is a complaint in 46% of climacteric women, fatigue in 38%. Libido may decline over months to years but not in all cases.

Women born in the United States now live to 80 years of age, with menopause occurring at an average age of 51.4 years. With more than one-third of adult life spent in estrogen deficiency, the long-term problems of osteoporosis and accelerated atherosclerosis loom ever larger in society.

Treatment of Acute Natural Menopause

While the acute symptoms of menopause can be treated by modest estrogen dosages, such as 0.3 mg conjugated equine estrogens (CEE) daily, this dosage will not prevent osteoporosis. Thus, it makes little sense to treat with less than minimum replacement dosages of 0.625 mg. Mild tranquilizers can be employed as useful adjuncts if anxiety predominates, but are inappropriate in depression. Depression may be obvious, often occurring spasmodically and to great depths, even with suicidality, or covert, masked by the irritability attendant to acute menopause. Antidepressant medication may be appropriate.

Atrophic vaginitis and symptoms of bladder and urethral irritation must be occasionally treated in a woman who is not a candidate for long-term estrogen replacement. Systemic symptoms respond to the vaginal estrogen, and the contraindications apply as with oral therapy, to be discussed. Six months is the maximum such a program should be pursued before a decision to institute a full hormone replacement or to discontinue estrogen.

SURGICAL MENOPAUSE

Surgical menopause is distinguished not only by rapidity of onset but by distinct physiologic sequelae. In natural menopause, the

ovaries, exhausted of ova themselves remain intact, continuing to produce testosterone. In surgical menopause, there is absolute loss of both ovarian estrogen and ovarian testosterone, source of approximately one-half of circulating testosterone.

The commonly encountered decline in libido after hysterectomy may be related more to falling testosterone than to estrogen loss (1). This phenomenon often occurs even after "subtotal" (ovary sparing) hysterectomy, due to ovarian atrophy following compromise of ovarian blood supply in surgery.

Treatment of Surgical Menopause

Management of the acute phase is the same as that of acute natural menopause except that the patient should be briefed regarding the postoperative menopausal symptoms, noting that they are likely to differ from those of natural menopause. After total (nonovary sparing) hysterectomy in the absence of contraindications, estrogen replacement therapy (ERT) should proceed in a standard protocol. Progesterone opposition to estrogen is not necessary because of the absence of the endometrium.

In other countries and to an increasing extent in the United States, an estrogen/androgen preparation such as Estratest (esterified estrogens and methyl testosterone), to be mentioned later, is among other treatment protocols (2). Other acceptable regimens are discussed later in the section on prevention and treatment. Thus, the patient should be educated as to possible change in libido and the availability of an androgen-containing regimen within a few weeks of surgical recovery. If one or both ovaries is (are) spared in a physiologically premenopausal female, the patient may be observed while educating her to the possibilities of later onset of estrogen deficiency and delayed decrease in libido. FSH levels would be checked every 6 months or in the event of any symptoms of estrogen deficiency. If FSH rises prematurely, owing to ischemia of the ovaries, she should be placed on standard ERT while following closely her sexual adjustment, taking care to counsel the patient as well as her partner.

LONG-TERM SEQUELAE OF MENOPAUSE

Atherosclerosis after Menopause

Table 19.1 shows the main causes of death in postmenopausal females, with coronary artery disease (CAD) in the forefront.

Table 19.1.

Cumulative mortality owing to four conditions per 100,000 population for women (to age 75): expected and predicted after postmenopausal HRT.

Condition	Mortality Expected (no.)	Projected Mortality from HRT (no.)	Relative Risk from HRT
Coronary artery disease	10,500	5,250	0.5
Osteoporosis—fractures	938	419	0.5
Endometrial carcinoma	188	37	0.2
Carcinoma of breast (postmenopause)	1,406	2,250	1.6
Total (net relative risk)	13,032	7,956	0.61

HRT = hormone replacement with estrogen cycled with a progestogen.

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Estrogen has favorable effects on total and high density lipoprotein cholesterol (TC and HDLC), lowering the former and raising the latter. The average woman's HDLC is around 50, compared with men's at about 40 mg/dL (1.03 mmol/L). Postmenopausal women have more coronary artery disease than do premenopausal age peers, a situation significantly prevented by estrogen replacement. In a large retrospective study, the common postmenopausal reversion to android habitus and weight gain were prevented by estrogen replacement (3). While progestogen derived from 19 nortestosterone (e.g., norethindrone), when used in hormone replacement therapy (HRT), reverses some of the beneficial effects on lipids, this is not the case with C-21 derived progestogens, such as medroxyprogesterone acetate (Provera). It has been estimated that HRT or estrogen replacement therapy (ERT) can prevent roughly half of the CAD deaths in postmenopausal women (4). HRT/ERT is dealt with later, under osteoporosis by convention. Based on the number of lives saved, however, postmenopausal HRT is perhaps more germane to prevention of CAD.

Osteoporosis

Osteoporosis is correctly defined as increased bone porosity due to thinning of bony trabeculae brought about by bone resorption outpacing new bone formation. However, it is appropriate to refer to the overall decrease in bone density that occurs with age as

osteopenia since other pathologic processes are involved, e.g., secondary hyperparathyroidism and osteomalacia. The former is caused by the loss of parathormone inhibiting effects of estrogen and the latter, a decrease in calcification of the osteoid matrix. With the advent of dual energy x-ray scanning (Dexa), a different usage of these two terms has crept into the vocabulary, to be discussed later. Finally, most clinicians continue to use the term osteoporosis generically to encompass the total process.

Fifty percent of cancellous bone and 5% of cortical bone disappears during the era of 40 to 80 years of age, during which period pathologic fractures and those following minimal trauma increasingly beset women (5). Eleven percent of women incur vertebral fractures between the ages of 45 and 65 (5), and females carry a cumulative lifetime risk of 46% for this fracture; 24% for Colles fractures, and 9% for fractures of the pelvis. Hip fractures, the greatest cause of morbidity and mortality, accelerate in incidence at about the age of 65. Untreated women who live to the age of 85 have a lifetime risk of 33% for hip fracture, which continues to carry up to a 20% first-year mortality.

Risk factors for osteoporosis, besides female sex, are small body build, Northern European or Oriental race (probably based on smaller peak bone mass), smoking, sedentary life style, poor nutrition, and various underlying medical conditions. The latter have in common immobility (e.g., rheumatoid arthritis), certain medications, and hypercortisolism (e.g., Cushing's disease or iatrogenic glucocorticoid). Smoking is as powerful a risk factor as estrogen is protective. It is estimated that fracture rates can be reduced by 50% through the use of HRT/ERT. This would have the effect of reducing the lifetime cumulative mortality due to hip fracture from 6% to 3%.

Prevention and Screening of Osteoporosis. Primary prevention without screening is superior to secondary prevention after screening and is accomplished by educating young women to exercise adequately, not to smoke, to maintain dietary calcium at 1.5 grams/day, and to prepare them positively for the prospect of HRT or ERT toward the arrival of menopause. Secondary prevention consists of the same approach for those who exhibit signs such as increased thoracic kyphosis and the initiation of hormone replacement in the proper setting, and is dealt with later in this section. The regimens utilized in primary prevention after menopause are listed below.

Calcium Maintenance. Oral calcium is a necessary part of every preventative regimen but in itself is not impressive for prevention of osteopenia. Intake adequate to assure 1.5 gm/day is required. The average daily consumption by the American female is 600 mg, so most clinicians prescribe 1 gm/day of elemental calcium. Calcium carbonate in 250 mg 5 times per day or 500 mg tablets twice daily is available as Oscal or in chewable antacid forms such as Tums, which contain 200 mg (5 time per day) or 500 mg (twice daily).

Hormone Replacement Therapy. HRT refers to postmenopausal daily estrogen and concomitant progesterone, the latter to counter the effect of unopposed estrogen to cause endometrial hyperplasia and carcinoma. Opposing estrogen replacement with a cycled or daily progesterone preparation is in fact statistically protective against endometrial carcinoma (6). HRT/ERT is the most potent available postmenopausal regimen for prevention of osteoporosis and postmenopausal acceleration of CAD. Recent reports indicate that HRT/ERT delays the onset of senile dementia and that women who take postmenopausal estrogens have mental functioning superior to those who do not (7). In currently acceptable protocols, HRT/ERT does not cause blood pressure elevation.

A waning controversy continues regarding the question of whether ERT/HRT increases the risk of breast cancer. A Swedish group reported that patients who had taken estrogen had a higher rate of breast cancer than those who had not (8). The study group, except for a small cohort, had taken ethinylestradiol in 50 g dosages, much more potent than approved dosages of CEE and comparable preparations used in the United States for HRT/ERT. Another study found no increased risk in users of contraceptive pills containing ethinylestradiol, even in presence of family histories of breast cancer (9). An as yet unpublished survey of 422,373 women, funded by the American Cancer Society's Cancer Prevention Study II in 1982, comparing breast cancer mortality with the rate found in the National Death Index, showed a 16% lower rate in estrogen users. This held for those taking estrogen for more than 10 years, and the risk reduction was highest, 35%, in those who started with HRT/ERT before age 40 (10). In terms of potency per unit dosage, oral contraceptive estrogen dosages are 5 to 8 times those normally employed in postmenopausal replacement protocols (Table 19.2).

Table 19.2.**Biologic potencies and dosages for estrogen preparations used for long-term HRT.**

Preparation	Relative Biologic Potency	Range of Typical Dose (mg)
Piperazine estrone sulfate (Ogen)	1.0	0.35–1.50/day
Estradiol, oral, micronized (Estrace)	1.2	1–2/day
Estradiol, transdermal (Estraderm)	10.0	0.05 or 0.10 twice weekly
Conjugated estrogens (Premarin)	2.6	0.625–1.250/day
Esterified estrogens (Estratab, Menest)	2.6	0.625–1.250/day
Ethinylestradiol ^a (Estinyl, Feminone)	496.5	0.02–0.05/day

^aAlso used in multiple contraceptive combinations.

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The most liberal estimate of relative risk of breast cancer mortality in postmenopausal hormone replacement is 1.6 across all ages after menopause (11). Assuming this is true, if atherosclerosis mortality can be reduced by 50% and hip fracture mortality by 50% by the use of ERT/HRT, the saving in absolute mortality favors estrogen replacement by nearly 9:1 (Table 19.1).

For ERT or HRT to succeed, the patient must be accepting, informed, and therefore motivated. Pregnancy must be ruled out even if the patient is experiencing vaginal bleeding; a baseline mammogram should have been accomplished within the prior 12 months; pelvic examination is done to establish normal anatomy; Papanicolou smear is done, and in some cases endometrial biopsy, if indicated (as in postmenopausal bleeding); thyroid function studies may be helpful if acute menopausal symptoms suggest thyrotoxicosis.

Standard protocols:

1. Hormone replacement therapy (HRT), appropriate for menopausal females with intact uteri and endometria:

- a. Cycled estrogen, e.g., conjugated equine estrogens (Premarin) 0.625 mg daily for 25 days/month; a progestogen overlapping the last or first 10 to 14 days/month of a 25-day estrogen cycle (e.g., medroxyprogesterone acetate [MPA, Provera] 5 mg daily). On this protocol the patient goes the last 5 days of the month without any medication. Withdrawal bleeding normally occurs during the 5 days without medication, and usually ceases by the end of 6 to 9 months, requiring longer treatment in women whose HRT has been initiated within a few months after clinical menopause by the foregoing definitions, and less in older women who have not experienced vaginal bleeding for long periods. Reassurance and explanation may greatly facilitate patient acceptance in those who are reluctant to tolerate return of "menstrual periods." The foregoing notwithstanding, if breakthrough bleeding continues for 6 months, or somewhat longer for withdrawal bleeding during hormone-free intervals of cycled estrogen protocols, an endometrial biopsy must be done to rule out endometrial carcinoma.
 - b. Daily estrogen, usually CEE 0.625 mg daily without break, and a progestogen simultaneously daily (e.g., medroxyprogesterone acetate 2.5 mg). Breakthrough bleeding occurs early with the unbroken daily schedule but generally ceases by the end of 6 months. Again, reassurance and forewarning may facilitate acceptance and compliance. After 6 months of continued withdrawal bleeding, an endometrial biopsy should be performed to rule out endometrial carcinoma.
 - c. Combinations of CEE 0.625 mg and MPA 2.5 mg in one pill (e.g., PremPro) taken daily, or CEE 0.625 mg in a 28-day pack containing 14 days of MPA in addition (Prem-Phase) are now available.
 - d. Transdermal estrogen may be given daily, month around, but the progestogen must still be given orally when the uterus is present. A disadvantage is that the estrogen misses the first pass through the liver and consequently loses much of the lipid remediating effects.
2. Estrogen replacement therapy (ERT), appropriate only if the patient has undergone hysterectomy or otherwise possesses no uterus:
 - a. Daily estrogen, usually CEE 0.625 mg daily without break. A progestogen is not indicated, nor is there any evidence

that such medication would be protective against development of breast carcinoma.

- b. Transdermal estrogen may be given daily, month around, without opposing progestogen with the disadvantage of estrogen missing the first pass through the liver. The other estrogens listed in Table 19.2 may be used in cyclic regimens in their recommended dosages. Rarely, estradiol levels may be utilized to assess therapeutic success.

Less utilized is the estrogen/testosterone combination Estratest (1.25 mg esterified estrogens and 2.5 mg methyl testosterone), which may be given daily 25 days on, 5 days off, for surgical menopause in the acute and subacute phases. It is of value in cases wherein libido has fallen notably after surgery. At present, it is approved for only 6 months and should be succeeded by other standard HRT protocols.

Timing of initiation of HRT/ERT and period of commitment:

ERT/HRT should be started as soon as menopause is diagnosable, based on history and $\text{FSH} \geq 20 \text{ pg/mL}$, or is eminent as adjudged by the clinical setting. The first 3-year period appears to be crucial for prevention of initial decline in bone density. No upper limit of age has been set for continuation of HRT/ERT, except for patients acceptance of the inconvenience of taking pills.

Most would not initiate HRT after age 65.

Contraindications:

They are unexplained vaginal bleeding; chronically impaired liver function; acute thromboembolic disease, including thrombophlebitis, pulmonary embolism, acute myocardial infarction, and stroke; past history of thromboembolic disease if patient were taking hormones at the time, including contraceptives; and history of breast or endometrial carcinoma. Unopposed estrogen, given long-term, confers a risk of endometrial carcinoma, which disappears when estrogen is taken along with progestational agents. ERT/HRT conveys a relative risk of cholecystitis of 2:3.

Alternatives to Estrogens.

Diphosphonates:

The diphosphonates were originally exploited for their actions to inhibit both bone resorption and mineralization and were used in Paget's disease of bone (as etidronate, Didronel). Newer agents include pamidronate, tiludronate, and alendronate

(12), the latter available as Fosamax, which may be taken orally on a convenient 10 mg daily dosing basis and appears to be free of the gastrointestinal side effects attendant to other members of the family. In the vertebral fracture study arm of the fracture intervention trial (FIT), alendronate has been shown to reduce relative risk of vertebral body fractures in postmenopausal females by 48%/year, increase bone density, and to retard loss of height (13). The clinical fracture rate arm of the FIT study, not yet published but presented in 1996 in Amsterdam, has found that alendronate taken over the 3-year intervention period results in a 51% reduction of hip fracture incidence, comparable to the rate reduction effected by HRT/ERT (14). Diphosphonates have the advantage of not being contraindicated in breast cancer. They should not be used in the presence of hypocalcemia. While alendronate may be promoted soon for use in primary prevention, most endocrinologists feel it should be reserved for cases in which estrogens are either refused or contraindicated.

Calcitonin:

Calcitonin has been used in Paget's disease of bone and was utilized mostly in "pathologic" states, in which medical conditions such as glucocorticoid use have resulted in osteoporotic fractures. It is proven effective for control of bone pain of virtually any benign or malignant cause, including pain of osteoporosis. It is now available as salmon calcitonin in a nasal spray under the trade name Miacalcin. However, its only proven application is for bone pain, which in the case of postmenopausal osteoporosis, is due to repeated microfractures. It is prescribed as 200 to 400 IU per day. Except in situations of long-term exposure to systemic glucocorticoids, research on fracture prevention has yet to be completed, as of this writing. In the near future, it will probably be shown to reduce fracture rates as a preventive measure in osteoporosis.

Fluoride:

Though advocated intermittently for more than 20 years, it has never been accepted as standard therapy for prevention of osteoporosis. Fluoride has been shown to increase bone density but is fraught with gastrointestinal and arthralgic side effects. It causes bone fragility along with increased density. A new formulation of monofluorophosphate may solve many of the problems associated with it.

Tamoxifen:

This competitive inhibitor of estrogen is indicated as maintenance therapy for estrogen receptor-positive breast cancer.

As such, it exhibits estrogenic activities at a less potent level, including remedial effects on lipids, proliferative effects on endometrium, mixed effects on vaginal epithelium, and preventive effects on postmenopausal osteoporosis, the latter about 40% of the potency of estrogen. In the United States, it is approved only for breast cancer tertiary prevention. Research may be directed increasingly toward its use in primary prevention of breast cancer, beginning in the postmenopausal era in women at high risk for breast cancer (15).

Assessing Risk. Risk assessment, based on sex, body build, smoking, etc., is reliable to discover high-risk patients but not as reliable for mild to moderate cases. Bone density measurement at the present time is best used in research or clinically to motivate high-risk patients. Routine screening is still not considered cost effective, nor necessary. When a patient is considered to be at high risk, assessment by dual photon absorptiometry has now been replaced by dual energy x-ray. Bone density can be accurately measured and compared with mean peak density for the individuals height and weight at the age of 30. Greater than one and less than 2 1/2 standard deviations (SD) below the mean is defined as osteopenia (a linguistic violence to the former generic use of the Greek-based root referring all pathophysiologic contributions to the process). More than 2 1/2 SD below the mean at age 30 is defined as "osteoporosis," or severe osteopenic disease.

Much is being written about biochemical markers for increased bone resorption, such as collagen cross-links and their associated peptides, earlier and more sensitive indicators. Pyridinoline and deoxypyridinoline urine assays, if found to be elevated, indicate increased bone collagen breakdown, hence, osteoclastic activity presumed to be outstripping osteoblastic activity. Test charges run roughly \$50, and it remains to be seen whether they offer more than does risk assessment.

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Diseases of the Breast

Marjorie A. Bowman and Marcia B. Szewczyk

DISEASES OF THE BREAST

Examination

Little information is available on which methods of breast examination find cancers more frequently. Most physicians agree, however, that the breast examination should include: visual inspection (dimpling or swelling are worrisome signs); direct palpation in a circular fashion to be certain all areas of the breast have been examined; direct palpation of the nipple and area beneath the nipple, and axillary palpation. Palpation can be done directly against the chest wall and by examining the breast off the chest wall between the fingers.

Screening for Breast Cancer

Whether to screen for breast cancer is not controversial, but “how,” “when,” and “for whom” are.

A mammogram is a radiologic screening technique that works better in fatty, compared with dense (more fibroglandular breast tissue), breasts. Breasts become more fatty with age and are more dense during premenopause or while on hormone replacement therapy. The clearest group of women who benefit from mammographic screening are those over 50, probably up to age 65, maybe age 70. It is estimated that screening women in this age range reduces breast cancer deaths by about a quarter (1). Screening 10,000 women aged 50 to 70 annually is estimated to result in 2 to 6 fewer deaths (1 in 1700 to 1 in 5000 screened) (2).

The National Institutes of Health has changed its recommendation and is no longer recommending mammograms for women in their 40s (3). This is because of a meta-analysis of studies in women in their 40s that found no significant improvement in the rate of breast cancer mortality; the relative risk of mortality for screened 40- to 49-year-old women was 0.93 with the 95% confidence interval including the value of 1 (0.76 to 1.13) (1). Other groups, such as the American Cancer Society, continue to recommend mammograms for women in their 40s.

The U. S. Preventive Services Task Force (4) currently recommends mammograms every 1 to 2 years for women ages 50 to 69. The evidence for clinical breast examination every year is less clear, and the Task Force did not recommend for or against it. Similarly, the Task Force found insufficient evidence to recommend for or against teaching women self-breast exam. "There is limited and conflicting evidence regarding clinical benefit of mammography or CBE for women aged 70 to 74 and no evidence regarding benefit for women over age 75; however, recommendations for screening women aged 70 and over who have a reasonable life expectancy may be made based on other grounds, such as the high burden of suffering in this age group and the lack of evidence of differences in mammogram test characteristics in older women versus those aged 50 to 69." Consistent with this, Harris and Leininger (5) suggest that an older woman who is expected to live 8 to 10 years may benefit from mammographic screening. How often to screen is also unclear. Screening intervals ranging from 12 to 33 months have shown effectiveness (6). Medicare, however, provides reimbursement only for biennial screening in women over age 65.

Most clinicians feel that patients who are at high risk for breast cancer should be screened more aggressively. Patients who are considered high risk include those with a significant family history (2 or more first-degree relatives with breast cancer, especially if the cancer occurred premenopause or was bilateral) and those with atypical hyperplasia, carcinoma-in-situ, or previous breast cancer. Although no conclusive studies have been done in these populations, recommendations encourage monthly self-breast exam and annual mammographic screening beginning in the fourth decade. Less clear are recommendations for clinical breast exam, with recommendations ranging from every fourth month to annually (6, 7).

Mastalgia/Breast Pain

Mastalgia or mastodynia, i.e., breast pain, is very common, particularly in the child-bearing years during the premenstruum. Breast pain is an uncommon symptom of breast cancer and is usually from benign causes. Mastalgia is often divided into cyclic and noncyclic. Most cyclic breast pain is thought to be due to hormonal changes. One or both breasts may be painful. Most postmenopausal mastalgia is from hormone replacement therapy. Contrary to public opinion, most patients with mastalgia do not have cysts in the breast. All women with breast pain should have a thorough breast and axillary examination and consideration for mammogram as indicated.

A low-fat, low-caffeine diet often helps with cyclic mastalgia. Appropriately fitted support bras may also make a difference. It is uncommon to require medication for breast pain. The majority of women can tolerate the discomfort if reassured that they do not have cancer. When medication is needed, some women find low-dose birth control pills (8) or minor pain relievers helpful. Evening primrose oil and vitamins E and B6 are often suggested, but evidence is insufficient to support their use. In severe cases, danazol is the first and only FDA-approved option, followed by bromocriptine, tamoxifen, or GnRH agonists. These agents should only be used for several months to a year before a trial off medication, because of the induced hypoestrogenic state and the unknown long-term effects. Bilateral subcutaneous mastectomy is the final, rare, resort. Depression should be considered in women with severe mastalgia (9).

Noncyclic pain occurs in 1 out of 10 women with severe pain thought by the woman to originate in the breast (10). It may be localized or diffuse and is unlikely to be hormonal and may not respond to medication. It is more likely to be anatomic and may not originate from the breasts. Examination with the patient upright and leaning forward can sometimes differentiate between chest wall pain and breast pain. Costochondritis is probably the most common illness presenting with apparent breast pain, but other considerations include heart disease, herpes zoster, and referred musculoskeletal pain.

Mastitis also is a cause of breast pain and presents with pain, erythema, and fever. Therapy consists of antibiotics that cover the most common pathogens: strep, staph, and *E. coli*. The lactating woman should continue to breast feed to ensure adequate emptying of the breasts.

During breast feeding, pain is also commonly associated with superficial *Candida* fungal infections. This responds to antifungal therapy, and, once again, breast feeding should be continued.

Discharges

A small amount of discharge can often be expressed with pressure on the nipple and areola. This is considered normal. Nipple discharge is more likely to be from benign causes than malignant disease. Abnormal discharges include spontaneous discharges and expressible discharges that have an unusual appearance.

Bloody discharges are the most worrisome, as up to one-fourth are caused by a cancer (11), although the most common cause is actually benign intraductal papilloma. The older the patient, the more likely cancer is the cause. The blood content can be confirmed by a Hemastix or observing the discharge layer out on cotton gauze. Many patients will have a palpable mass, which should be biopsied or removed. In general, breast exams and mammograms should be completed for all patients. Ultrasounds may be helpful. A Pap smear of the discharge can be performed, but has a high false-negative rate. For those without a mass, and with a negative exam and mammogram, a galactogram or exploration is indicated. The exception is the pregnant or lactating woman, where a small amount of blood may not be as significant.

Milky discharges (galactorrhea) are usually bilateral and hormonal in origin. Benign causes are pregnancy, the postpartum period (up to 1 to 2 years), and mechanical stimulation. Pathologic hormonal causes include pituitary adenoma (in which case, the prolactin level would be elevated), endocrine diseases (hypothyroidism or Cushing's syndrome), and chronic renal failure. Drugs, such as birth control pills, tricyclic antidepressants, cimetidine, metoclopramide, and phenothiazines, also cause galactorrhea. Trauma, recent surgery, or herpes zoster can cause transient galactorrhea.

Purulent discharges are from infections, often a mastitis in a lactating woman, although they can occur at other times as well. Treatment consists of warm compresses and appropriate antibiotics. If mastitis occurs in an elderly woman, an underlying cancer should be suspected.

Other discharges create more of a diagnostic dilemma. A green-black discharge or one of mixed color (but not a bloody

discharge) often originates from ductal ectasia. This discharge is frequently bilateral and from several ducts in a parous woman. No treatment is uniformly recommended. Nipple hygiene may be all that is required, and surgery may be successful. If an inflammatory component is present, antibiotics (12) and anti-inflammatories may be helpful. Sero-sanguinous, clear, or watery discharges tend to have causes similar to bloody discharges. Any discharge other than a milky discharge indicates the need for breast exam, mammography, and close follow-up with possible surgical exploration. Discharge from a single duct is also more worrisome for cancer.

Masses and Mammographic Abnormalities

Masses are discovered more commonly by the patient than by the physician on routine exam. The majority of masses will be from benign causes such as cysts and fibroadenomas, but cancer must be considered whenever a woman presents with a mass.

Most masses in very young women are fibroadenomas; the usual is a round, mobile, nontender firm mass. If mammography and/or ultrasound confirm the typical appearance of a fibroadenoma, then removal becomes elective. However, mammograms are often of little use in women under age 25. Some physicians also perform fine-needle biopsy for confirmation.

The most common breast mass in premenopausal women is the macrocyst (cyst >3 mm in size), particularly if ultrasounds are performed and nonpalpable small cysts can be seen. Some cysts, especially larger ones, are associated with tenderness and pain. Treatment for the pain associated with cysts is the same as for mastodynia, except that sometimes cysts are aspirated. Most cysts are in the upper outer quadrants of the breasts. The term fibrocystic disease is a description used to refer to cysts, lumpiness, or other breast symptoms. Because of its vagueness, it is of little clinical significance. Physicians should use more specific terms when possible.

For a mass that feels cystic (round, regular, and somewhat compressible), needle aspiration can be performed simply in the office if the remainder of the examination is benign (i.e., there are no skin or nipple changes and no axillary adenopathy). A 23- or 24-gauge needle with a 10 cc syringe is used; a pop can often be felt when the needle enters the cyst. If the mass entirely disappears when the fluid is aspirated and the fluid is not bloody,

then only one follow-up visit to confirm the absence of a mass is needed. Another alternative for a mass that feels cystic is to wait through a menstrual period and recheck the mass in the week following the next menstrual period. Many cystic masses will disappear during this time.

With a remaining mass, or in women of advanced age, further work-up such as mammogram, ultrasound, and/or biopsy is indicated. Most cysts are themselves benign, but women with many cysts are at a modestly increased risk of breast cancer.

Masses may also be caused by hematomas and/or fat necrosis secondary to trauma. In general, these masses will disappear within 4 to 6 weeks.

Diagnostics tools to evaluate breast masses include mammography, ultrasound, aspiration, and biopsy. One needs to remember that palpable masses may not always be identified on mammography. A palpable mass that is not a cyst without clear characteristics of fibroadenoma requires biopsy. The biopsy options are fine-needle aspiration, stereotactic, or an open biopsy (usually an outpatient procedure). For nonpalpable mammographic abnormalities, the radiologist's interpretation is paramount in determining the need for further work-up. For potentially suspicious mammographic abnormalities, needle-localization or stereotactic core biopsies are often used. Stereotactic core biopsies require special, expensive equipment, and are not available everywhere.

Fine-needle biopsy is thought to have good sensitivity and specificity, but is very operator and center dependent (13). Sensitivities and specificities can be more than 90% (13, 14). The larger stereotactic core biopsies probably have a slightly better sensitivity and specificity. With any biopsy a chance remains that a significant lesion was missed. Thus even with a negative biopsy, close follow-up is indicated.

Other Breast Cancer Signs

Many palpable abnormalities are not readily classified as a mass. What some patients feel cannot be felt by the physician. Other findings feel like a thickening, or are vague. Careful exam, clinical judgment and close follow-up are indicated. Skin dimpling or retraction is usually associated with cancer, but is also occasionally seen with benign disorders.

Crusting or erosion of the nipple (usually not extending out onto the breast skin) is Paget's disease of the breast, which rep-

resents underlying cancer. Erythema of the breast is the earliest sign of Paget's disease and must be differentiated from dermatitis. Inflammatory breast cancer may also present with erythema of the nipple or breast tissue and can be confused with mastitis; if in doubt, do a biopsy.

Breast Cancer

Breast cancer is very common, occurring in 1 of 8 or 9 women over a lifetime. About one-quarter of the U.S. breast cancers occur in women under age 50, but the prevalence increases with age, with almost half of the breast cancers occurring in women over age 65. The evidence concerning the relationship of hormone replacement therapy to the incidence of breast cancer is controversial and is as yet unresolved.

Women at high risk for breast cancer (actually a small percentage of women) need special consideration in terms of counseling, monitoring, and possibly prevention. Only 15% of patients with breast cancer have a positive family history and only 5% have hereditary breast cancer. Genetic screening may soon be available for this subset of women and may help guide those who wish to consider prophylactic mastectomy. Patients at high risk for cancer need more aggressive screening. Research is also under way to look at the role of tamoxifen in primary prevention in addition to its current use to prevent breast cancer recurrence (15).

Because of the prevalence of breast cancer, most physicians will see many breast cancer patients. Once breast cancer is found, one role of the primary-care physician is to ensure that the patient has been provided adequate information to make decisions about treatment plans. For example, in many cases, breast conservation procedures such as lumpectomy with axillary node dissection followed by radiation therapy result in identical outcomes when compared with more extensive surgical therapy (16). Medical exceptions to the use of breast conservation procedures include cancers larger than 5 centimeters, a multifocal lesion, and an extensive intraductal component. Women with either very large or very small breasts may have more cosmetic issues concerning surgery versus radiation therapy. Chemotherapy and endocrine therapy, usually with tamoxifen up to 5 years, are also options. The primary-care physician also needs to arrange care and provide emotional support. Breast cancer support groups are available in most communities.

Breast Implants

Many women have had breast implants for cosmetic or postsurgical reasons. Silicone implants were common until recently, but because of controversy over the possibility that the silicone was associated with rheumatologic disease, particularly scleroderma, few silicone implants are being placed today. Even though large medical studies (17) do not support an association between silicone implants and scleroderma, a large liability suit has been proceeding through the courts. In 1993, the FDA ruled that information on the safety of silicone implants was insufficient, and that all new implants were to be done in research studies only. For women who think their implants are a cause of symptoms, removal is an option, but it exposes the patients to the risks of general anesthesia, loss of breast tissue, blood loss and financial expense with possible poor cosmetic results. Saline implants are an alternative with no known association with scleroderma.

In general, women with implants are not at increased risk of breast cancer although mammography is technically more difficult. Mammograms should be ordered routinely; the radiologist should be informed that the implant is present.

CONCLUSION

All woman of appropriate age groups and health status should be screened for breast cancer. Many women will present with breast symptoms or signs. The physician should ascertain benign versus malignant causes and treat appropriately.

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Problems Unique to Males

Chapter 21

Genitourinary Problems of the Male

Steven W. Strode

BLADDER PROBLEMS OF THE MALE

Cystitis and Urethritis

Isolated cystitis is rare in healthy men, and a documented bladder infection merits a genitourinary evaluation following treatment. The length of the urethra helps to protect older boys and men from infections of the bladder. See Chapter 16 for coverage of cystitis and urethritis in males, including sexually transmitted diseases.

Urinary Incontinence

As in women, the prevalence of urinary incontinence in men increases with age. Estimates of this problem in males between 25 and 64 years old vary between 1% and 5%. Among noninstitutionalized elderly men, urinary incontinence probably affects 20%. However,

more than half of male nursing home patients have some degree of incontinence, and this problem may have been significant in the decision to place them in the nursing home (1). Men (and women) may assume the leakage of urine is a part of aging and therefore not mention the condition to their physician unless asked.

Urge incontinence, usually associated with detrusor instability, accounts for two-thirds of cases. It can occur with advanced benign prostatic hypertrophy (BPH) due to irritative phenomena and progress later to obstructive retention and overflow incontinence. Other causes of bladder irritation and urge incontinence include cystitis, bladder tumors, and kidney stones. Spastic bladder, a form of neurogenic bladder, consists of sudden detrusor contractions due to an upper motor neuron lesion. Typical causes are stroke, cerebral palsy, paraplegia, and multiple sclerosis. Conversely, lower motor neuron lesions produce a flaccid bladder and overflow incontinence. This can occur in diabetes mellitus, certain herniated disk and spinal cord lesions, and some cases of Parkinson's disease (2). Stress incontinence in men is unusual. In the absence of postoperative complications, this finding should trigger a search for spinal nerve root lesions. Underlying cognitive and physical impairments could lead to functional incontinence, a diagnosis of exclusion.

Postvoiding residual urine measurement (measured catheterized urine volume after voiding a full bladder), normally less than 50 ml, is increased in outlet obstruction (e.g., BPH) or flaccid bladder but is normal in spastic bladder and stress incontinence. In general, urge incontinence or bladder spasticity can be treated by timed voiding and with anticholinergic agents (oxybutynin [Ditropan] 2.5 to 5 mg three times a day or propantheline [Pro-Banthine] 7.5 to 30 mg three times a day). This type of medication, however, must be avoided with BPH and other obstructive conditions of the urinary or gastrointestinal tracts. Flaccid bladder treatment should focus on the underlying cause. Sometimes catheterization is required, preferably on an intermittent basis. A resource for patients with complicated cases or combinations of types of incontinence is the AHCPR Clinical Practice Guideline (3).

PROSTATITIS

Prostatitis can be acute or chronic. Chronic prostatitis (which is more common than acute prostatitis) is classified as bacterial, nonbacterial, and prostatodynia. The latter may present with uri-

nary frequency, urgency, dysuria, perineal discomfort, low back pain, body aches, and occasionally hematospermia.

Acute Prostatitis

Acute prostatitis may present with acute onset of high fever, chills, malaise, and body aches. Urinary tract symptoms of frequency, urgency, and dysuria may occur with pain in the perineum, rectum, or sacrococcygeal area. Acute urinary retention can develop. The prostate is very tender, boggy, and warm. Prostate massage should not be done for it may induce bacteremia. Urethral catheterization, though potentially liable on the same basis, may be unavoidable due to urinary retention. Some would recommend resorting to percutaneous suprapubic drainage. Gram-negative enteric bacteria are the usual offending organism. The patient's bladder may be infected with the same bacteria, so a urine culture should be collected. The patient who appears toxic will be best served with hospitalization for intravenous fluids, analgesics, antipyretics, stool softeners, and parenteral antibiotics until the patient is responsive and stable. Ampicillin with an aminoglycoside is appropriate until culture and sensitivity results are available. Less severely ill patients are likely to respond to oral agents such as trimethoprim-sulfamethoxazole or a fluorquinolone such as ciprofloxacin. Treatment should be continued for 4 to 6 weeks.

Prostatic abscess, relatively uncommon, is suggested when a patient (especially a diabetic) with acute prostatitis or a urinary tract infection develops a spiking fever with rectal pain and persisting leukocytosis in spite of appropriate antibiotic treatment. A firm, tender, or fluctuant mass may be felt in the prostate. *Escherichia coli* or anaerobes are usually present. Treatment involves surgical drainage and antibiotics (4).

Chronic Bacterial Prostatitis

The acute onset and fever of acute prostatitis are absent. The physical examination is usually unremarkable in all three chronic prostate conditions. Chronic bacterial prostatitis is characterized by the persistence of pathogenic bacteria (Gram-negative enteric bacteria and, perhaps, mycoplasma and chlamydia) in prostatic fluid.

Diagnosis is made by fractionated voided bladder specimens—the four-bottle technique. The first voided specimen measures

urethral urine, and a midstream specimen measures bladder urine. The third specimen is expressed prostatic secretions produced by prostate massage. The fourth and final specimen is urine voided immediately after the prostate massage. Chronic bacterial prostatitis produces positive cultures and increased number of WBCs in the third or fourth specimens, while the cultures of the first and second specimens are negative. Positive cultures in the first or second specimens indicate a primary cystitis or cystitis accompanying the chronic prostatitis.

Antibiotics penetrate the chronically infected prostate poorly. Oral trimethoprim/sulfamethoxazole 160 mg/800 mg 2 times a day (Bactrim or Septra DS), or ciprofloxacin 250 to 500 mg 2 times a day, or doxycycline 100 mg 2 times a day are appropriate options. Therapy should be continued for 6 to 12 weeks. Even with this length of treatment, the responsible organism may be eradicated from prostatic secretions in only 30% to 40% of cases. Cultures of prostatic secretions should be periodically secured for 1 year following treatment. If infected prostatic calculi are present, surgical removal may be curative. Suspected gonococcal prostatitis warrants a single IM injection of ceftriaxone (Rocephin) 250 mg, in addition.

Nonbacterial Prostatitis

Men suffering from this condition have the same symptoms as chronic bacterial prostatitis, but they do not have bouts of cystitis, and cultures of all the fractionated voided bladder specimens are negative. Signs of prostate inflammation are evident: Expressed prostatic secretions show 10 or more white blood cells per high-power microscope field. Warm sitz baths, nonsteroidal anti-inflammatory drugs (NSAIDs), and possibly antispasmodics may provide symptomatic relief. Empiric treatment with long-term tetracycline or erythromycin to cover mycoplasma and chlamydia is controversial.

Prostatodynia

The symptoms are the same for this condition as for the other two forms of chronic prostatitis. In prostatodynia, no findings of inflammation are seen in expressed prostatic secretions and no positive cultures of fractionated voided bladder specimens. Tension myalgia of the pelvic floor or spasm of the external urethral

sphincter may be responsible for the symptoms. Warm sitz baths are recommended. Drug treatment with NSAIDs, the alpha-blocker prazosin (1 mg twice a day) or baclofen (5 to 10 mg 3 times a day) may be helpful.

BENIGN PROSTATIC HYPERTROPHY

The prostate gland has three growth spurts: prior to birth, puberty, and at advanced age. After puberty, the gland measures an average of 3.4 cm in length, 4.4 cm in width and 2.6 cm in depth. The enlargement of advancing age involves both glandular and stromal elements. On autopsy, 40% of men in their 50s show evidence of benign prostatic hypertrophy (BPH). Almost 90% of men in their 80s show evidence (5). The only clearly established risk factors are age and normal testicular function. The size of the prostate on digital rectal examination is not always indicative of the degree of bladder outlet obstruction.

The bladder responds to the outlet obstruction with symptoms that collectively define "prostatism": frequency, dribbling, nocturia, hesitancy, and intermittence of voiding. When these develop gradually in a man over age 40, they suggest benign prostatic hypertrophy. Acute onset of prostatism in a man 40 years old or under is likely due to acute prostatitis. Over this age, an acute onset must raise consideration of carcinoma of the prostate. In 10% to 15%, prostate enlargement is clinically silent until urinary retention is the presenting symptom. In a man with BPH, urinary retention may be triggered by use of alcohol, anticholinergics, decongestants, and cough medicines (4).

Diagnosis of Benign Prostatic Hypertrophy

The American Urological Association Symptom Index is becoming the standard method to assess and follow symptoms of BPH (6). The index is a series of seven questions. Scores are classified as mild (0 to 7), moderate (8 to 19), or severe (20 to 35) (Table 21.1). Other useful tests are urinalysis and serum creatinine, the latter to assess renal function in the care of obstruction. Postvoid residual urine volume and urodynamic studies are optional tests. Greater than 150 ml on the postvoid residual volume is considered abnormal. The Benign Prostatic Hypertrophy Clinical Practice Guideline (7) views the prostate specific antigen (PSA) as another optional test. The current PSA cannot discriminate between those

Table 21.1.
The AUA symptom index.

Question	Not at All	Less Than 1 Time in 5	Less Than Half the Time	About Half the Time	More Than Half the Time	Almost Always
1. During the last month or so, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. During the last month or so, how often have you had to urinate again less than 2 hours after you finished urinating?	0	1	2	3	4	5
3. During the last month or so, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5
4. During the last month or so, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. During the last month or so, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. During the last month or so, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
7. During the last month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	None	1 Time	2 Times	3 Times	4 Times	5 or More times
	0	1	2	3	4	5

AUA symptom score = sum of question 1 to 7.

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with elevated levels from symptomatic BPH and those with prostate cancer. Imaging studies are not needed in the absence of other urinary tract problems.

Treatment of Benign Prostatic Hypertrophy

Treatment of the asymptomatic or minimally inconvenienced patient is rarely needed. Those with obstruction to the point of urinary retention or with other complications are best treated surgically. Physicians should assist all the patients between the extremes in considering the options of treatment or watchful waiting.

Transurethral resection of the prostate is the most commonly used surgical procedure, although open prostatectomy may be best if the prostate is quite large. Transurethral incision of the prostate can be performed when the gland is small, when preservation of potency and normal ejaculation is an important consideration and when the patient is debilitated (6). Other minimally invasive surgical treatments under investigation are prostatic stents, balloon dilation, microwave therapy, and laser prostatectomy.

The natural history of BPH continues to be poorly understood. Progression of symptoms is not inevitable. Watchful waiting for the man with mild or moderate symptom scores may be the best course for many. Alpha adrenergic blocking drugs reduce the smooth muscle tone of the prostate, its capsule, and the bladder neck so that urinary flow increases. The antihypertensive medications terazosin, prazosin, and doxazosin all have this potentially beneficial side effect; onset of action is rapid, and they have no effect on PSA levels. Men with hypertension and significant BPH symptoms may be able to be treated with one drug for both conditions. The most common side effects are orthostatic hypotension, dizziness, tiredness, and nasal congestion. Long-term effectiveness of the medications for treating BPH has not yet been reported. Starting doses are terazosin (1 mg at bedtime), prazosin (1 mg 2 or 3 times daily) and doxazosin (1 mg once daily). Alpha blockers can be used with finasteride.

Finasteride (Proscar) blocks the conversion of testosterone to dihydrotestosterone by inhibiting 5-alpha-reductase. Finasteride can reduce the size of large prostates by up to 50%. Dosage is 5 mg daily, with few side effects, but they include impotence and decreased libido. Maximum symptomatic benefit may not be

seen for 6 to 12 months. Finasteride causes a 50% decrease in PSA concentrations, so clinical judgments of PSA in men on this medication should be based on half the usual upper limit of normal of PSA (6). Long-term effectiveness of finasteride is also not yet known. Pregnant women and those of childbearing potential should avoid contact with finasteride pills and the semen of men taking the drug.

BENIGN CONDITIONS OF THE TESTICLES

Scrotal pain can be caused by masses, inflammation, epididymitis, sperm granuloma, trauma, or testicular torsion. Pain can be referred to the scrotum from ureteral stones, inguinal hernias, or genitofemoral and ilioinguinal nerves (T10—L1) (8).

Orchitis

Viruses are the most common pathogens of orchitis, and mumps is the most frequent viral cause. Unlike other infections of the male genitourinary system, the pathogens of orchitis are usually blood-borne. Orchitis is less common than epididymitis or prostatitis, but it occurs in 20% to 35% of postpubertal men who acquire mumps. With mumps, onset of orchitis is usually 4 to 6 days after the appearance of parotitis. Only one testicle is involved in 70% of cases. Sterility follows in about 10%. Granulomatous orchitis can arise from infections with tuberculosis, fungi, or actinomycosis. Bacteria can spread from an infected epididymis, or orchitis may result from trauma.

The testicle in orchitis is tense, swollen, and tender. An associated hydrocele may be present. Bed rest, scrotal support, analgesics, and local cold application will help provide symptomatic relief. If improvement does not occur within 10 days, consideration should be given to an abscess and to a testicular tumor (9).

Epididymitis

Epididymitis is the most common cause of inflammation within the scrotum in all but the pediatric age group (less than 18 years of age). A painful unilateral scrotal swelling usually develops over 2 or 3 days. Dysuria, urinary frequency, fever, chills, and malaise are often present. A hydrocele may form. Up to the age of 35, epididymitis is usually due to a sexually transmitted pathogen, most commonly *Neisseria gonorrhea* or *Chlamydia trachomatis*, com-

plicating about 1% of gonococcal urethritis. In older men, enteric Gram-negative bacteria spread from an infected prostate. Bed rest, scrotal elevation, local cold application, and NSAIDs are useful for symptom relief regardless of the etiology. When sexually transmitted infection is suspected, the preferred treatment is ceftriaxone (250 mg intramuscularly) plus doxycycline 100 mg orally twice a day for 10 days. The older male with fever should be hospitalized and started on intravenous aminoglycoside or cephalosporin. The older male without signs of sepsis may respond to trimethoprim/sulfamethoxazole 160/800 mg twice a day for 2 weeks. The male should be followed with periodic examinations to ensure that the scrotal contents return to normal to exclude a testicular tumor.

Undescended Testicle

One or both testicles are undescended in 3% to 5% of newborns. This is more likely to occur in the premature, low birth weight, small for gestational age, and twin infant. In most of these boys, the testicles do descend by 3 months of age. Careful examination of a calm and warm infant is needed, as what may at first appear to be an undescended testicle may be a testicle retracted by the cremasteric muscle. The incidence of undescended testicles is 0.8% at 9 months of age and also at postpubertal ages. Intervention is most appropriate at 1 or 2 years of age. Surgical treatment by orchiopexy allows for future testicular examinations, may reduce the risk of testicular cancer, provides cosmetic and psychological benefits, and may help to preserve fertility. With uncorrected cryptorchidism, infertility is as high as 90%. After orchiopexy in infancy, infertility rates may fall to 40%. Cryptorchid testicles are believed to be at a 10- to 40-fold greater risk of malignancy. Lifetime risks of testicular cancer are 3.5% to 5% in a man with undescended testicles and no correction (versus an expected rate of 0.22% in a man without a history of delayed testicular descent) (10). Since orchiopexy may not completely reduce this risk, some experts recommend periodic ultrasound examinations of operated undescended testicles (11).

Torsion of the Testicle

Although torsion of the testicle can occur at any age, it is most likely to occur in the first year of life and in midadolescence. Torsion is

uncommon after age 30. Undescended testicles are more prone to torsion. Onset may be sudden or gradual. The pain is usually in one side of the scrotum and may be associated with groin, lower abdominal, or flank pain. Often, nausea and vomiting occur. The affected testicle is elevated and tender. The scrotum may be edematous. Urinalysis is typically unremarkable.

Other diagnoses to consider in the setting of an acute scrotum are epididymitis, torsion of the appendix testis, acute scrotal (angioneurotic) edema, idiopathic scrotal fat necrosis, an acute hemorrhage into a testicular neoplasm, orchitis, Henoch-Schoenlein purpura, testicular abscess, acute incarcerated inguinal hernia, traumatic hydrocele, and traumatic testicular rupture (12). Testicular scanning with technetium may be helpful in confirming the diagnosis but should be performed within 1 hour of presentation. A Doppler stethoscope can be used to listen for the presence or absence of arterial flow to the testis although false results can occur.

The definitive treatment is bilateral fixation orchiopexy, as the contralateral testicle is at increased risk of later torsion. Testicular viability of 50% to 100% is possible if surgery is performed within 10 hours of the onset of symptoms.

Torsion of the appendix testis is associated with less pain and vomiting. Peak incidence occurs at 10 years of age and is rare after puberty. A firm tender nodule at the upper pole of the testis may be palpable. When the diagnosis is certain, operative treatment is not needed. Symptomatic relief can be provided with bed rest, scrotal elevation, local cold, and analgesics. If there is any question of testicular torsion, prompt surgical exploration is required.

Other Benign Conditions of the Testicle and Scrotum

A hydrocele results from fluid accumulation in the potential space between the tunica vaginalis and the tunica albuginea anterior to the testicle. If the processus vaginalis is patent, the hydrocele will communicate with the peritoneum. Most pediatric hydroceles are communicating and will close spontaneously by the end of the first year of life. In adulthood, most hydroceles are asymptomatic. When they do cause discomfort, it is felt as heaviness in the scrotum, pain in the inguinal area, or lower back pain. Hydroceles usually feel cystic but may be tense. They will transilluminate, while inguinal hernias will not. When a large hydrocele prevents palpation of the testicle, ultrasound can be used. If the

hydrocele becomes infected, causes pain, or presents a cosmetic problem, it should be surgically repaired.

A varicocele is a dilation of the veins of the pampiniform plexus above the testicle in the spermatic cord. This occurs more commonly on the left side. Rare before puberty, varicoceles are found in up to 15% of men and up to one-third of men evaluated in infertility evaluations. Although there are usually no symptoms, there may be a dull scrotal discomfort. When the patient is examined standing, the varicocele feels like a "bag of worms" and increases in size with the Valsalva maneuver. Repair of the varicocele in adolescence is advisable if the testicle on the affected side is 0.5 cm smaller than the other testicle. Surgical repair, even in an adult, may improve fertility.

A spermatocele is a common benign cyst of the epididymitis. It may be solitary or multiple. Most are smaller than 1 cm diameter and should be freely movable. Only large spermatoceles cause any discomfort, so reassurance is often the best treatment (13).

PROBLEMS OF MALE SEXUAL DYSFUNCTION

The most common sexual dysfunctions in men are impotence and premature ejaculation. As sexual dysfunctions are thought to occur at some time in as many as half of sexual relationships and since patients may be reticent to initiate conversations with their physicians about sexual concerns, the doctor should include questions about sexual function in routine health maintenance examinations. Three suggested questions for men are: (a) Are you currently sexually active?; (b) Are you satisfied with your sex life?; and (c) Do you have difficulty obtaining an erection or controlling ejaculation? (14).

Erectile Dysfunction (Impotence)

Erectile dysfunction is the consistent inability to obtain and sustain an erection that is satisfactory for intercourse. Vascular problems can arise from arteries or veins. Arterial compromise may be from large or small vessels. Small arterial compromise is common in diabetics and the elderly. Neurologic causes include multiple sclerosis, diabetes mellitus, alcoholic neuropathy, and head or spinal cord injury. Hormonal causes result in inadequate testosterone levels. Testosterone levels are decreased by chromosome abnormalities, toxins, gonadal injury, pituitary trauma or tumor, hypothyroidism, Addison's disease and Cushing's syndrome. Me-

chanical problems can result from chromosomal abnormalities and Peyronie's disease. Many drugs can lead to erectile dysfunction including antihypertensives, anticholinergics, antipsychotics, sedatives, antihistamines, H₂ receptor antagonists, digitalis, alcohol, and recreational drugs. Psychogenic conditions of depression, anxiety (especially sexual performance anxiety), anger, and stress cause erectile dysfunction.

It is important that men not confuse the normal changes of aging for sexual dysfunction. As men age, increased time and stimulation are required for an erection and erections are not as firm. More time is needed to attain a second erection after ejaculation (refractory period). More stimulation is required to reach orgasm, which may be less intense. Sexual arousal is more subject to distraction, fatigue, and anxiety. Detumescence occurs more quickly upon cessation of stimulation.

Factors that suggest a psychogenic cause are the presence of nocturnal or early morning erections, erections during masturbation, abrupt onset, and impotence in only certain situations. The physical examination should include examination of the vascular system, a neurologic exam, thyroid palpation, evaluation of penis and testes, and a check of gynecomastia. If decreased libido or bilateral testicular atrophy occurs, then endocrine testing is needed (15). Urologists can check penile blood pressure and perform nocturnal penile tumescence monitoring. An intracavernous injection of papaverine is the best screening tool for vascular impotence, but the incidence of single-use papaverine-induced priapism is 4% (16).

Patients and their partners benefit from education about the human sexual response cycle and common misconceptions. Sensate focus behavioral therapy is a plan for "homework" where intercourse is initially proscribed while the couple concentrates on specific sensate focus exercises. Yohimbine is an alpha 2 agonist available in pill form. Central nervous system excitement is the major side effect, so it should be avoided if the patient has any cardiovascular system problems. Data are mixed as to whether yohimbine is more effective than placebo. Vacuum constriction devices draw blood into the penis and hold it there with a specially designed tourniquet. They are contraindicated in patients on anticoagulants or with sickle cell disease. Penile self-injection with vasoactive substances such as papaverine will lead to induced erections that last about an hour. Patients must be trained and

observed in the technique. Side effects include hematoma, fibrosis, nodules or pain at the injection site, and priapism. Self-injection should not be used in patients with transient ischemic attacks, hypotension, sickle cell disease or trait, or penile venous compromise (17). Penile implants come in semirigid, malleable and inflatable types. Infection, perforation, and mechanical failure can occur.

Premature Ejaculation

Premature ejaculation is ejaculation that occurs before the man or his partner is ready for intercourse to end. It is usually due to psychogenic causes such as anxiety, discord in the relationship, or prolonged periods of sexual abstinence. Rare organic causes are trauma to the sympathetic nervous system from pelvic fracture or abdominal aortic aneurysm surgery, prostatitis, urethritis, and narcotic withdrawal (16). Treatment is education about the sexual cycle and training the man to gain voluntary control over ejaculation. Two methods of training are the start-stop technique (17) and the squeeze technique of Masters and Johnson (18).

CARCINOMA OF THE PROSTATE

Prostate cancer is the most commonly diagnosed malignancy among American men and has the second highest mortality rate (following lung cancer). An estimated 244,000 men were diagnosed with prostate cancer in 1995, with more than 40,000 deaths predicted to be caused by that disease in the same year. African-American men have the highest incidence in the world (19). The incidence increases with age. Autopsy studies find that more than 30% of men over age 50 have microscopic collections of well-differentiated occult cancer cells in their prostate. The incidence of these foci increase to 50% by 70 years of age. Apparently, more than 90% of prostate cancers remain latent. The frequency of latent prostate cancer and the difficulty of predicting the 10% of prostate cancers that will progress complicate screening for this disease.

Early prostate cancer has no symptoms. More than 50% of prostate cancers are diagnosed after the disease has spread beyond the prostatic capsule. No evidence has been found that benign prostatic hypertrophy predisposes to prostate cancer. The cancer can present with symptoms of urinary stream obstruction

or even urinary retention. Low back pain or hip pain may result from local spread or metastases.

Prostate Cancer Screening

The examining finger can palpate only the posterior and lateral parts of the prostate gland. Up to 50% of cancers occur in parts of the gland inaccessible to digital rectal examination (DRE). A bony hard spot is a relatively late finding. Even a spot of induration should be referred for biopsy.

Prostatic specific antigen (PSA) is highly sensitive but not very specific. Benign prostatic hypertrophy will raise the PSA level. Although urinary tract infection, prostate massage, or prostate biopsy will cause elevation of the PSA level for at least 6 weeks, a typically conducted prostate examination will not adversely affect the PSA (20). Studies fractionating the PSA may result in evidence of improved specificity. Prostatic acid phosphatase has a much lower sensitivity. Transrectal ultrasound is helpful in evaluating patients with urological symptoms, an abnormal DRE, or elevated PSA. It is not advocated as a screening tool for prostate cancer.

Prostate cancer screening presents two significant problems. One problem is the inability of any current screening test, or combination of screening tests, to adequately differentiate the 90% of prostate cancers that will likely remain dormant from the aggressive 10%. The second problem is the lack of conclusive evidence that early detection and treatment improve survival. The American Cancer Society recommends an annual DRE beginning at age 40 and annual PSA for men 50 years old and older. The Society suggests annual PSA tests beginning at 40 years old for African-American men and men with a family history of prostate cancer. The U.S. Preventive Services Task Force does not recommend routine screening of prostate cancer with any modality (21). The clinician might discuss the controversy with his or her older male patients and let the patient join into the decision-making as to whether to use screening tests for prostate cancer. Prostate cancer screening for men with a life expectancy of less than 10 years is probably not worthwhile.

Prostate Cancer Staging and Treatment

The most common staging system for prostate cancer is that of the American Urologic Association. In Stage A, no palpable le-

sion is present. These are usually discovered on analysis of tissue from a prostate resection for benign prostatic hypertrophy. If the cancer cells are well differentiated, the rate of progression of prostate cancer is only 15% to 20% in 10 years. Survival may be little different from the expected survival based on age of the patient alone. Stage B cancer is confined to the prostate. The 5-year survival rate in studies varies from 54% to 88%. Disease is localized to the periprostatic area in Stage C. Here, the 5-year survival rate runs between 15% and 72%. Stage D cancer has metastasized with 5-year survival rates of only 6% to 30% (22).

Clinical staging usually involves an intravenous pyelogram, cystoscopy, serum acid phosphatase, bone scan, chest x-ray, and prostate ultrasound. PSA levels can be used to follow the response to therapy. Stage A cancers can be treated with radical prostatectomy or radiation therapy. Stage B cancers are usually treated with radical prostatectomy. Radiation therapy is the standard for Stage C cancers. Hormonal treatment is used for metastatic disease, either orchiectomy or diethylstilbesterol. Hormonal treatments help relieve pain but have not been shown to increase survival. Spot palliative radiation treatment can reduce pain from isolated bony metastases. Chemotherapy has not been shown to be effective at any stage of prostate cancer.

EVALUATION AND MANAGEMENT OF SCROTAL ENLARGEMENT

The common benign masses of the scrotum are spermatocele, hydrocele, and varicocele. A history of orchiopexy should increase the concern for testicular cancer. A history of prior mumps orchitis or testicular trauma may explain a size differential between testes. Sperm granulomas can occur after vasectomy. They are nodules, usually tender, at the site of the surgery. Ultrasound is valuable in differentiating causes of scrotal enlargement.

Malignant Tumors of the Testicles

A mass in the scrotum must be considered a tumor until proved otherwise. Testicular tumors can occur at any age, although the most typical age is between 15 and 35 years old. All men should be taught testicular self-examination techniques, ideally in junior high or high school. Primary-care providers should inquire as to the accomplishment of this monthly self-examination in men of the age at greatest risk as they would inquire of women as to

monthly breast self-examination. Each year in the United States about 6000 cases of testicular tumors are diagnosed. They are the most common malignancy in men of this age group. Testicular tumors usually present as a painless mass, but 15% to 20% present with epididymitis. It is very important to follow a person treated for epididymitis or orchitis to assure that the condition heals with no abnormality to the testes.

Cryptorchid testes are 10 to 40 times more likely to develop testicular cancer. About 10% of men who develop this malignancy will have a prior history of undescended testicles. The contralateral normally descended testicle of a man with a history of cryptorchidism also is at increased risk.

Although most commonly asymptomatic, a testicular tumor can present with a dull ache in the lower abdomen or scrotum. Less commonly, testicular pain may be present. Presenting symptoms of metastases are even less frequent. These symptoms include a neck mass, pulmonary symptoms, or an epigastric mass. Germ cell tumors will produce gynecomastia in about 5% of patients by production of hormones. If an examination of the testes yields suspicious findings, an ultrasound should be done. Ultrasound is effective in differentiating a hydrocele or epididymitis. Unless the ultrasound clearly excludes the possibility of testicular cancer, the patient should be referred to a urologist.

Testicular tumors in young children are usually germ cell tumors and most frequently yolk sac tumors. These generally occur in boys less than 2 years old. The younger the patient at the time of diagnosis, the better the prognosis. Staging is accomplished as in the adult, and successful treatment is frequently achieved with radical orchiectomy alone (23).

Testicular cancer is one of the most curable solid tumors. Surgical treatment is needed for all types and consists of radical inguinal orchiectomy with early clamping of the spermatic cord. A scrotal approach would contaminate scrotal lymphatics. Limited retroperitoneal lymph node dissection is often done at the time of orchiectomy. In the traditional staging system, Stage A means the tumor is confined to the testicle. In Stage B, the tumor has spread to retroperitoneal lymph nodes but not beyond. Metastases occur above the diaphragm or in the abdominal viscera in Stage C. Chest x-ray, computerized tomography, and tumor markers are helpful in the staging process. Alpha-fetoprotein and human chorionic gonadotropin are useful tumor markers for prog-

nosis and treatment. High initial levels of either indicate a poorer prognosis. Lactic dehydrogenase is also used as a less specific tumor marker. After orchiectomy, persistent elevation of any of these three tumor markers suggests residual cancer.

Seminoma

Seminomas are the most common type of testicular tumor. They are radiosensitive, so orchiectomy is usually followed with adjuvant radiotherapy. Seminomas are also sensitive to chemotherapy. Advanced seminomas are treated with multiple-drug cisplatin-based chemotherapy. The overall cure rate for all stages should exceed 90% (24).

Nonseminomatous Germ Cell Tumors

Nonseminomatous germ cell tumors include embryonal cell carcinomas, yolk sac carcinomas, choriocarcinomas, teratomas, and teratocarcinomas. They are not radiosensitive. Chemotherapy may be used following orchiectomy and retroperitoneal lymph node dissection. Stage A nonseminomas have a 5-year survival rate of 96% to 100%. Stage B nonseminomas have a 5-year survival rate of 90%. In Stage C, the nonseminomas have a 5-year survival rate between 55% and 80% (25).

Nongermin Cell Tumors

Stromal cell tumors include Sertoli cell tumors, Leydig cell tumors, and mixed gonadoblastoma tumors. All together, they account for only 3% to 4% of all testicular tumors. Metastatic tumors to the testes are rare. Lymphoma in the testes comprises less than 5% of all testicular tumors and is usually seen in men over 50 years old.

Patient Follow-up for Testicular Cancer

Although recommended regimens vary as to the frequency of follow-up examinations, all agree that the patient should be followed closely for the first 2 years (visits from every 1 to 3 months) and then biannually for 3 more years. Lifetime surveillance on an annual basis is then needed. The routine examinations should include chest x-ray, complete blood count, tumor markers, and interval history and physical. Scrotal ultrasound, including the remaining testicle,

should be done annually and some experts suggest periodic computerized tomography of the chest and abdomen.

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Musculoskeletal and Connective Tissue Problems

Chapter 22

Musculoskeletal Problems of the Neck and Back

Christopher G. Maropis

NECK PAIN

Neck pain may affect one-third of the adult population from time to time and may persist for 6 months or longer in 10% to 15% of these people (1). Neck injuries and neck pain most commonly are a result of motor vehicle accidents and falls. The majority of the rest are related to contact/collision sports (2).

When evaluating the patient with neck pain that is posttraumatic, questions regarding the mechanism of injury must be ascertained along with the presence of any associated weakness, numbness, or tingling.

A complete physical examination of the neck should include the anterior soft tissues, glands, and blood vessels. After the cervical area is inspected, the midline posterior cervical spine should be palpated followed by palpation of the paracervical musculature. Active range of motion should be checked in six directions: flexion, extension, left and right lateral flexion (all to about 45 degrees), and left and right lateral rotation (80 to 90 degrees), as should strength about the neck in these same directions. Thereafter, a thorough neurological examination of the upper extremities should be performed.

Torticollis

Torticollis, which is due to awkward positioning of the neck over several hours, is the most common cause of neck pain in adolescents and young adults. The typical presentation is an insidious onset of unilateral neck pain with limitation of one rotational movement, with the neck fixed in ipsilateral side flexion and rotation away from the affected side. A simple history regarding sleep positions and the use of one or more pillows that promote prolonged neck flexion may easily elucidate the condition (3).

The physical examination should include a search for neck adenopathy and a supraclavicular fossa and axillary examination to rule out a mass. Otherwise, the examination is essentially normal except for the above-mentioned limitation of motion and occasional tender and prominent sternocleidomastoid and trapezius muscles. Diagnostic studies are generally not indicated.

Therapy consists of a soft cervical collar for a few days along with relative rest, moist heat, NSAIDs as needed for pain, and a cervical contour pillow for sleep at night. The condition is most often self-limited and usually resolves within a week (4).

Cervical Ligament Sprain (Whiplash)

The single most common cause of neck pain is a hyperextension injury (whiplash) (3). This injury most often occurs as a result of a rear-end motor vehicle collision but can also occur in collision sports when a blow forces an athlete's neck into sudden extension. Upon rear impact, the patient's body is thrust forward, causing the head to suddenly fall backward into forceful extension that exceeds the limits of physiologic extension and excursion. This sudden mechanism causes the cervical ligaments to be

stretched or torn. The most common site of cervical sprain is C7-T1 (4). Upon presentation, the patient usually complains of local pain in the midline of the posterior neck along with stiffness, interscapular pain, arm pain, and/or occipital headache. In addition, a severe hyperextension injury may result in dysphagia, blurred vision, tinnitus, dizziness, Horner's syndrome, diplopia, cognitive impairment, or temporomandibular joint injury (5).

On physical examination, neck flexion and extension will be decreased, and a palpable defect may be noted above or below the vertebra prominence at C7-T1 (5). Presence of normal crepitus between the larynx and vertebral column rules against a hematoma. A full cervical x-ray series including lateral flexion and extension views should be done to exclude fracture or facet dislocation and to assess stability. The retropharyngeal soft-tissue shadow should not exceed 3 mm anterior to C3. A shadow greater than 6 mm is evidence for a hematoma. A small avulsion fracture of the anteroinferior vertebral body is a positive sign of an anterior ligamentous disruption. Though the partial loss of the normal cervical lordosis is thought to be of no significance, an acute kyphosis is thought to portend a worse prognosis, as is a preexisting spondylosis (5).

Therapy for a cervical sprain initially includes rest, ice, immobilization with a soft cervical collar, and NSAIDs as needed for pain. Severe injuries may require bed rest to remove the weight of the head from the neck muscles and ligaments. The cervical collar should not be worn for more than 2 weeks nor should passive physical therapy modalities be used since both may encourage dependence, and impair recovery. Isometric exercises should be done frequently each day for flexors, extensors and lateral flexors of the neck. Range of motion (ROM) exercises should be initiated once the acute symptoms have started to subside (3).

In this era of litigation, it is becoming more and more common for symptoms to persist into the subacute and chronic phase. In these patients, physical therapy may play a more important role. Antidepressants may also prove beneficial and have the added effect of improving sleep. The prognosis for these patients often depends on the outcome of their litigation (6).

The most worrisome complications of cervical sprain are progressive instability and persistence of pain. About 40% of patients may continue to have pain for up to 7 to 10 years after the initial injury (6, 7).

Cervical Radiculopathy

The nerve root is vulnerable to compression by three structures: the facet joint, the uncovertebral joints, and the disc. The most common cause of nerve root compression is a herniated disc, followed by cervical spondylosis. The most commonly involved nerve roots are the sixth and seventh cervical roots, which are caused by C5–6 or C6–7 disc herniation or spondylosis; these account for about 90% of all cases (8). Table 22.1 lists the deficits present with various root involvements.

The evaluation of a patient suspected of having cervical nerve root compression includes an attempt to ascertain any precipitating cause, distribution, duration and frequency of pain, paresthesia or weakness, occurrence with activity, and night pain. The vast majority of patients present with neck and arm pain with or without motor weakness or paresthesia, generally not preceded by trauma or any other known cause. Pain is usually in the cervical region, upper limb, shoulder, or interscapular region (8).

The physical examination is initiated by observing the patient’s neck position and movement. Obvious atrophy may help in “dating” the radiculopathy. Manual muscle testing must be performed to assess weakness, as should a full sensory examination and evaluation of deep tendon reflexes. The neck compression or Spurling’s test is performed by extending the neck and rotating the neck to the side of pain and applying downward

Table 22.1.
Abnormalities in cervical radiculopathy.

Level	Root	Sensory Symptoms	Motor Deficits	Reflexes
C4-C5	C5	Lateral arm	Shoulder abduction, external rotation	Decreased biceps
C5-C6	C6	Radial forearm, thumb, index finger	Elbow flexion, forearm supination	Decreased brachioradialis
C6-C7	C7	Middle finger	Elbow extension, wrist and finger extension	Decreased triceps
C7-T1	C8	Little finger, ulnar forearm	Finger and wrist flexion	Normal or decreased finger flexors

pressure on the head. This maneuver may cause or accentuate limb pain or paresthesia because neck extension causes posterior disc bulging, whereas lateral flexion and rotation narrow the ipsilateral neural foramina. This test, though of high specificity, has a low sensitivity.

X-rays should be obtained and include AP and lateral films with lateral flexion and extension views. Further imaging studies are reserved for patients whose symptoms and findings are not classic and lead to suspicion of other serious causes, or those who are not improving or who have progressing neurological deficits. If an imaging study is deemed necessary, an MRI would be the study of choice.

Electrodiagnostic studies can be helpful to facilitate the diagnosis and differentiate cervical radiculopathy from other syndromes. EMG signs of denervation increase in density for the first 3 to 4 weeks after the onset, so that this study can roughly date the lesion. In those with less severe findings, however, EMG should not be performed for at least 3 to 4 weeks after symptom onset.

In regards to treatment, no long-term outcome studies have compared operative to nonoperative treatment of cervical radiculopathy. The objective of treatment is to reduce or resolve the pain, improve or resolve any neurological deficits, and avoid spinal cord complications.

During the acute phase, the patient's activity should be modified, particularly if his or her job entails moderately heavy to heavy activities or the use of the neck in vulnerable positions such as extension and ipsilateral flexion and rotation. Neck positioning is also important. A rigid cervical collar can provide greater restriction of cervical motion than a soft cervical collar, but patients comply better with the more comfortable soft collar. The cervical collar should be worn as long as possible during the day, using comfort as a guide. As symptoms improve, it can be worn only while engaging in strenuous activities and while driving (8).

Heat or cold therapy can be used locally depending on whichever modality the patient feels is most beneficial. Traction, however, has an unproven efficacy and has been reported to cause TMJ problems.

Exercises such as simple range of motion movements should be avoided during the acute phase. NSAIDs should be used. Epidural steroids should be reserved for those who do not im-

prove with the above therapy. Conservative or nonoperative treatment will be effective in 80% to 90% of patients with proven cervical radiculopathy (8). Operative intervention is considered when sensory or motion deficit persists or pain intractable.

BACK PAIN

Back pain is second only to upper respiratory infection as a reason for an office visit to a primary-care physician. More than 75% of people at some time in their lives have severe low back pain that requires medical attention, with an annual incidence of 7% to 15%. Medical expenses directly related to back pain total more than \$8 billion per year. Disability payments and indirect expenses are more than double that amount. Low back pain is the leading cause of disability in people under age 50 and is second only to heart disease as a cause of disability in people over age 50. It results in the loss of more than 93 million work days each year (9).

Low Back Pain Evaluation

Low back pain can effectively be divided into one of three groups: a) potentially serious spinal conditions such as tumor, infection, fracture, or a major neurologic compromise such as cauda equina syndrome; b) back-related sciatica leg symptoms suggestive of lumbosacral nerve root compression, and c) non-specific back symptoms that do not suggest a serious condition or nerve root compromise. During the initial visit for a patient with back pain, an attempt should be made to seek a potentially dangerous underlying condition. Certain "red flags" (Table 22.2) during the history and physical can raise the suspicion of a serious underlying spinal condition. The absence of any "red flags" essentially rules out the need for any special studies during the first 4 weeks of symptoms, since 90% of patients will recover within this time period (10).

The history should include questions regarding the duration, quality, and character of the pain, any radiation of pain, numbness, weakness, or stiffness. In addition, the patient should be asked if he or she prefers to stand, sit, or lie down to palliate the pain and if he or she has had a previous back problem and any subsequent studies or operative procedures.

The physical examination should include careful observa-

Table 22.2.**“Red flags” for potentially serious conditions.**

Possible Fracture

Findings from medical history:

Major trauma, such as vehicle accident or fall from height

Minor trauma or even strenuous lifting (in older or potentially osteoporotic patients)

Possible Tumor or Infection

Findings from medical history:

Age over 50 years or under 20 years

History of cancer

Constitutional symptoms, such as recent fever or chills or unexplained weight loss

Risk factors for spinal infection, recent bacterial infection (e.g., urinary tract infection), intravenous drug use or immune suppression (from corticosteroid use, transplant or HIV infection)

Pain that is worse when in supine position, severe nighttime pain

Possible Cauda Equina Syndrome

Findings from medical history:

Saddle anesthesia

Recent onset of bladder dysfunction, such as urinary retention, increased frequency or overflow incontinence

Severe or progressive neurologic deficit in the lower extremity

Findings from physical examination:

Unexpected laxity of anal sphincter

Perianal / perineal sensory loss

Major motor weakness: quadriceps (knee extension weakness), ankle plantar flexors, evertors and dorsiflexors (foot drop)

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tion (gait, limping, posture), palpation of the lumbosacral spine and paralumbar musculature, motion at the waist in flexion, extension, lateral flexion and lateral rotation, and neurologic screening of the lower extremities. A thorough neurologic examination of the lower extremities would include assessment of strength, sensation, circumferential measurements to detect atrophy and deep tendon reflexes. Testing for tension of the sciatic nerve root should also be performed (discussed under radiculopathy).

Low Back Strains

Low back strains typically occur after unaccustomed physical activity or trauma. The low back pain seldom radiates below the knees, and signs of sciatic nerve compression are absent. Onset of pain may occur immediately or within a few hours after the insult or possibly not until the next day. The physical examination in such patients may uncover some stiffness with motion about the waist but otherwise is essentially negative.

Therapy for low back strains should include NSAIDs regularly for 5 to 7 days to minimize discomfort and encourage physical activity. Muscle relaxants, though still prescribed often for this entity, are of limited value and carry the additional risk of habituation with prolonged use. Ice can be used during the acute stage when heat would be contraindicated, but after 2 or 3 days, moist heat can be used if the patient feels it is beneficial. A day or two of relative rest may be advisable but strict bed rest is now believed to do more harm than good.

Failure to improve within 2 weeks indicates the need for further diagnostic evaluation for both occult organic disease and behavioral factors that may be impeding recovery such as life stress, mood disorder, or employment-related secondary or interpersonal gain (11).

Lumbar Radiculopathy

Though lumbar radiculopathy can occur secondary to degenerative lumbosacral disease as is the case in lumbar spondylosis, disc herniation is the most common cause. Disc herniation is the protrusion of gelatinous material of the disc (nucleus pulposus) through the annulus fibrosus. Herniation most often occurs through a posterolateral defect, but midline herniation also occurs. Greater than 95% of all disc disease and herniation occurs at the L4-5 or L5-S1 level.

Risk factors for lumbar disc disease include advanced age, vigorous exercise for more than 15 years or in people over 20 years of age, vigorous exercise for less than 1 year, sedentary work, history of trauma, male sex, obesity, and cigarette smoking. Patients usually present with back pain, referred leg pain, radicular leg pain, sensory changes, leg weakness, or a combination of these symptoms. The most common presenting symptom is severe low back pain and/or leg pain that develops immediately or within a few hours after an injury. The pain may be exacerbated

by spine flexion or by increased abdominal pressure (coughing, sneezing, straining). Radiation of pain below the knee suggests radiculopathy.

On physical examination, muscle spasm may limit spine mobility. In addition, there may be numbness, weakness or reflex changes noted in the lower extremities. A herniated L4–5 disc that compresses on the L5 nerve root typically leads to weakness in dorsiflexion of the great toe and foot along with hypesthesia of the dorsum of the foot. In contrast, a herniated L5–S1 disc that compromises the S1 nerve root may lead to a decreased ankle jerk reflex along with weakness in plantar flexion and hypesthesia of the lateral foot (Table 22.3).

The straight leg raising (SLR) test should be performed with the patient sitting and lying supine. The seated SLR test involves asking the patient to actively extend the involved leg at the knee and dorsiflex the foot to at least 90 degrees. A positive test is one in which pain is elicited in the posterior leg, which most often radiates below the knee and causes the patient to lean back in hip extension to decrease his or her symptoms of pain. The lying SLR test is performed by passively elevating the patient's involved leg with the patient supine. Characteristic radicular pain is only considered positive if it occurs between 30 and 60 degrees of hip flexion. Dorsiflexing the foot at the angle of pain should exacerbate the symptoms. An SLR on the uninvolved leg that produces pain in the involved leg occurs only 25% of the time but is much more specific for nerve root compression than the standard SLR test on the involved side.

Table 22.3.
Features of herniated lumbar discs.

Level	Root	Sensory (Pain or Numbness)	Motor (Weakness)	Reflexes
L3-L4	L4	Anteromedial thigh and knee	Quadriceps	Decreased knee jerk
L4-L5	L5	Lateral leg, first three toes	Dorsiflexion of foot and great toe	Decreased posterior tibial reflex
L5-S1	S1	Posterior leg, lateral heel	Plantar flexion of foot and great toe	Decreased ankle jerk

When a clinician suspects lumbar radiculopathy, he or she should obtain plain films. If further imaging studies are deemed necessary, an MRI would be the test of choice, since it has the advantages of being noninvasive with no radiation exposure.

The typical clinical course of lumbar radiculopathy is one of repeated remission and relapse over weeks to months. Cauda equina syndrome can occur in 1% to 16% of cases. This syndrome is characterized by compromised bowel and bladder function, saddle anesthesia (decreased penile, vaginal or rectal sensation), and bilateral leg pain and weakness. This entity should be considered a surgical emergency (9).

Management of lumbar radiculopathy includes bed rest on a firm mattress for no longer than a few days. Prolonged bed rest causes muscle weakness, cardiovascular decompensation, and bone demineralization. For this reason, brief periods of standing and walking during the prescribed bed rest should be advised. The sitting position increases intradiskal pressure to a level higher than it is in the standing position, so patients should be advised not to sit up in bed. If herniation occurs following an injury, then ice should be used initially for a maximum of 10 minutes at a time. After 2 or 3 days, heat can then be applied for no longer than 20 minutes at a time. Occupational therapy may prove useful in offering ways for the patient to engage in activities of daily living without causing back discomfort.

Since between 90% and 95% of patients will have a spontaneous resorption of herniated disc material and subsequent resolution of radicular pain, it is safe to continue conservative therapy for as long as 6 weeks. If radicular pain becomes the chief complaint, then an MRI or other imaging study should be considered. Interestingly, no significant difference in recovery has been found between those whose herniated discs resolved spontaneously and those whose herniated discs were surgically removed.

Only about 5% of patients require surgery. Surgery should never be performed for an asymptomatic herniated disc, and surgery is contraindicated in syndromes of back pain without accompanying radicular pain, paresthesias, or numbness.

Prevention of recurrences involves eliminating risk factors such as obesity and smoking. Moreover, regular endurance exercise and posture correction should be advised as should proper methods of lifting and performing manual labor (9).

Sacroiliac Problems

Sprains

Sacroiliac (SI) sprain syndrome is characterized by the acute onset of pain during torsional strain, tenderness over the affected SI joint, and relief of symptoms by infiltration of the joint with local anesthetic. Predisposing factors include certain situations that increase the risk of injury to the SI joints due to progressive softening and lengthening of the ligaments in the SI area. These situations include pregnancy, degenerative arthritis, and activities that require prolonged bending or lifting. In most cases, the mechanism of injury involves the act of straightening up from a stooped position. Postural defects such as pelvic inclination and/or excessive lumbar lordosis are associated findings (12).

Characteristic findings are pain over the SI joint or referred pain to the groin or posterior thigh. The pain intensifies when the patient lies on the affected side. Forward bending is limited and painful when the patient is standing, but improves when the patient is seated. The patient is most comfortable while sitting on the affected buttock. Tenderness is usually present over the involved SI joint and may also be over the buttock or posterior superior iliac spine. Many special tests are available to aid in diagnosing this entity (12). The most often used is Patrick's test, also known as FABER test, which stands for Flexion, ABduction and External Rotation of the hip. This maneuver is positive when it elicits pain over the involved SI joint.

Treatment for SI sprain syndrome involves relative rest, moist heat, and NSAIDs for discomfort and inflammation. Physical therapy may also be useful. In chronic cases, the SI joint may be injected with a combination of a corticosteroid and a local anesthetic. This syndrome most often resolves within 4 to 6 weeks (12).

Arthritis

Excessive SI ligamentous laxity and repeated displacements inevitably lead to osteoarthritis of the SI joint. Symptoms of this include local pain at rest, particularly upon awakening, stiffness, limited forward bending, and pain upon rising from a chair. Conservative treatment would include relative rest, moist heat, NSAIDs, occasional local injection, and a firm corset or brace. It is essential to differentiate this syndrome from degenerative

arthritis of the LS spine, which occurs in association with degenerative disc disease (13).

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Common Problems of the Upper Extremity

Amy Myers

Although a multitude of problems can affect the upper extremity, this chapter will focus on those injuries that commonly present to the family physician's office, emphasizing mechanism of injury, physical findings, and treatment. Familiarity with the anatomy and physical examination of the upper extremity are assumed for the purposes of this chapter.

SOFT TISSUE PROBLEMS

Shoulder

Impingement

Impingement syndrome, pain from compression of inflamed tissue between the humeral head and coracoacromial arch, is caused by any condition that narrows the subacromial space. This narrowing can be caused by structural abnormalities such as a curved or hooked acromion, degenerative changes within the glenohumeral or acromioclavicular (AC) joints, or more commonly from physiologic abnormalities such as inflammation and swelling of the rotator cuff (RTC) tendons, or overlying subacromial bursa.

The rotator cuff muscles (supraspinatus, infraspinatus, teres minor, and subscapularis) function primarily as stabilizers of the glenohumeral joint (a relatively unstable joint), in addition to assisting in abduction and rotation of the upper extremity. As stabilizers, they are under tremendous load in the overhead position when the joint is in its most vulnerable position. With repetitive

activity in this position (throwing sports, swimming, carpentry, house painting), especially if weakness or inflexibility of the RTC muscles is present, or underlying glenohumeral laxity, the RTC tendons may become inflamed and swollen, resulting in pain with compression against the coracoacromial arch. It is often difficult to distinguish between RTC tendonitis and subacromial bursitis, as the two are in such close proximity and are often affected similarly.

The pain of impingement is often insidious in onset, with associated stiffness and weakness in the shoulder. Often the pain is poorly localized ("feels deep inside") and is made worse with overhead activities. When severe, the patient may have difficulty sleeping secondary to pain.

On physical examination, there is pain through the most arduous arc (70 to 120°) of abduction, positive impingement and supraspinatus tests, and often rotator cuff and biceps weakness, compared with the opposite side. A positive impingement sign involves pain with forced internal rotation of a 90-degree forward flexed arm. A positive supraspinatus test involves pain and/or weakness with resistance against an internally rotated arm in the forward flexed and abducted position at 45 degrees. Radiographs are often normal but should be obtained if the patient has any history of trauma, or persistent symptoms, to rule out structural abnormalities.

Treatment for impingement includes relative rest (restriction of aggravating motion), use of ice and nonsteroidal anti-inflammatory drugs (NSAIDs) to reduce inflammation, and physical therapy to maximize range of motion and conditioning (flexibility, strength, endurance) of the RTC muscles. Corticosteroid injection into the subacromial space is often beneficial, but should not take the place of the above-mentioned therapy. Referral should be considered with failure of conservative therapy for more than 3 months with evidence of soft-tissue injury.

Glenohumeral Dislocation/Subluxation

A dislocation or subluxation of the glenohumeral joint involves a sprain of the glenohumeral ligaments and joint capsule. In a dislocation, there is complete loss of articular contact between the humerus and glenoid, whereas a subluxation involves increased translation of the humeral head relative to the glenoid, but contact of at least 50% remains. Since the vast majority of dis-

locations and subluxations occur anteriorly, the remaining focus will be on the anterior dislocation/subluxation.

The mechanism of injury for an anterior dislocation often involves either a direct blow to the posterior or posterolateral aspect of the shoulder with the shoulder in abduction, or secondary to a fall on an abducted arm. Although the vast majority of dislocations result from trauma, progressively less trauma is required if the patient has a history of prior dislocations, or multidirectional instability of the glenohumeral joint. Minimal trauma is usually involved for the subluxation, especially with a history of recurrent episodes.

The patient with an anterior dislocation will present with the affected arm being held by the opposite hand in slight abduction and external rotation. There is often a visible deformity with a prominent acromion, and the humeral head palpable anterior to the acromion and adjacent to the coracoid. If a subluxation has occurred, or if a dislocation has reduced itself prior to presentation, the patient will demonstrate a positive apprehension sign (resistance and apprehension with placing the shoulder in abduction, external rotation and extension), and laxity with anterior testing. Significantly increased multidirectional instability/laxity of the glenohumeral joint compared with the opposite side, or an abnormal “clicking,” or “popping,” on passive range of motion may indicate a glenoid labral tear or significant rotator cuff tear.

A thorough neurovascular examination should be performed before any attempt at relocation to rule out any neurovascular compromise. If readily available, AP, lateral, and modified axillary (West Point view) radiographs should be obtained pre- and postreduction. If radiology is not readily available, or if an experienced physician is comfortable with the situation, an attempt at reduction may be performed prior to radiographic evaluation.

On radiographic evaluation, one should note the position and direction of the dislocation as well as any associated fractures or bony defects, especially of the posterolateral humeral head (Hill-Sachs lesion) and anterior rim of the glenoid (Bankhart lesion). An MRI may be needed to rule out a glenoid labrum tear if suspected by physical examination. An MRI may be needed to rule out a glenoid labrum tear or large rotator cuff tear if suspected by physical examination, and the patient is not responding to conservative management.

After the physical examination and radiographic evaluation, if performed, an attempt should be made at reduction of the

dislocation. The chance of success is increased if the reduction is performed reasonably quickly after injury. A speedy reduction will also decrease the amount of muscle spasm and neurovascular compression. The following are the most commonly used techniques for reducing glenohumeral dislocations and subluxations:

Kocher maneuver: With the patient supine, the elbow externally rotated and flexed at 90 degrees, progressive traction is applied to the humerus followed by gentle adduction and internal rotation after relocation.

Stimson maneuver: A 5-pound weight is attached to the wrist of the affected arm with the patient prone and the affected arm hanging off the side of the table.

Traction/Countertraction (Rockwood maneuver): Gentle steady traction to the affected arm in 30- 45-degree abduction, with countertraction applied in the opposite direction with a sheet or swathe wrapped around the upper thorax.

After reduction has been obtained, the shoulder should be immobilized. Some authors prefer a strict 3- to 6-week period of immobilization (young athletes require a longer period because of an increased risk of recurrence, while chronic dislocators require a much shorter period of immobilization). Others feel the period of immobilization should be based on symptoms, with an early return to motion and rehabilitation when symptoms allow.

Following immobilization, rehabilitation involves range of motion, strengthening and conditioning of the RTC muscles. Return to activity can be allowed when the patient has achieved full range of motion, complete return of strength, and absence of pain. In cases of subluxation as opposed to dislocation, immobilization is seldom required.

Surgical stabilization is considered for individuals with recurrent episodes of either dislocation or subluxation.

Acromioclavicular (AC) Sprains

AC sprains involve stretching and/or disruption of the capsule and acromioclavicular ligament. The coracoclavicular ligament may also be disrupted in more severe sprains.

The mechanism of injury usually involves a direct blow to the lateral aspect of the shoulder, often by a fall where the lateral aspect of the shoulder impacts the ground. Patients with this injury will present with pain (worse with arm motion) and swelling at the AC joint. On physical examination, the distal

clavicle may ride above the level of the acromion. Tenderness may be present not only at the AC joint but also along the clavicle and at the trapezius and deltoid attachments. There will be pain with the crossover test (attempt to touch opposite shoulder with hand of the injured side), and with downward pressure on the distal clavicle.

In order to obtain a more objective evaluation of the distance of separation between the distal clavicle and acromion, AP radiographs should be performed with 5 to 10 pounds of weight held in each hand. AP view should include both AC joints to allow comparison.

Treatment of AC sprains involves ice, and sling for comfort, with an early return to motion. Healing time may take 2 to 6 weeks depending on the degree of injury. Surgical reduction and repair can be considered for persistent pain, or unsatisfactory reduction (primarily grade IV sprains where the clavicle has been displaced into the trapezius muscle).

Elbow

Lateral Epicondylitis (Tennis Elbow)

Tennis elbow is the most common presenting complaint for the elbow. It involves a strain or overuse of the extensor muscle group either at the muscle/tendon junction or the attachment site on the lateral epicondyle.

Insufficient muscle conditioning for a given activity, faulty mechanics, especially with racquet sports, and poorly fitted equipment (too small grip size, too tight racquet strings) are common risk factors for development of lateral epicondylitis. Although most commonly seen in racquet sports, it can also be seen in golf, fencing, throwing, weight lifting, and construction work.

Physical examination demonstrates tenderness over or just distal to the lateral epicondyle. There is demonstrable pain when wrist extension is resisted with the elbow in extension. There is pain and weakness with gripping (coffee cup sign).

Therapy incorporates relative rest (no grasping or lifting in pronation), ice, and NSAIDs, plus physical therapy for forearm conditioning. Iontophoresis (the use of an electric muscle stimulation unit to drive a medicine, usually a corticosteroid, across the skin to the affected area) produces good results, especially if incorporated early. Forearm or wrist splinting may provide some relief while the area is being reconditioned. A local steroid injection

may also be of benefit. Use of proper mechanics and equipment should be addressed throughout the therapeutic course. Referral for debridement can be considered if the above-mentioned conservative therapy fails.

Medial Epicondylitis (Golfer's Elbow)

Overuse or strain of the flexor pronator muscle group arising from the medial epicondyle results in medial epicondylitis.

On physical examination, the patient will have tenderness at the medial epicondyle. Pain is exacerbated by resisted wrist flexion and forearm pronation. Weakness in this area is often secondary to pain. Radiographs, if obtained, are often negative but may show small calcific deposits in the flexor pronator group.

Management of medial epicondylitis is very similar to that of lateral epicondylitis, with focus on the flexor group instead of the extensors. Ice, NSAIDs, forearm conditioning, with or without splinting, and occasional local steroid injection are the mainstays. The rare patient that does not improve may benefit from surgical referral.

Wrist and Hand

Carpal Tunnel Syndrome

This syndrome refers to symptomatic compression of the median nerve within the carpal tunnel of the wrist. Due to the bony walls and rigid fibrous roof of the carpal tunnel, any swelling within the tunnel can result in nerve compression. Repetitive hand motion resulting in inflammation and swelling of the flexor tendons is often the cause of this syndrome.

Patients often present with an intermittent or constant "tingling" sensation in the fingertips (especially the radial four fingers). One or all finger tips may be involved. The sensory changes tend to be especially prevalent at night and will often awaken the patient leading to shaking or moving of the hand in order to "wake it up." The discomfort may travel up the arm as far as the shoulder.

Special test results indicative of carpal tunnel syndrome on physical examination include Tinel's sign (pain with or without radiation with percussion over the carpal ligament), and Phalen's test (numbness, tingling, or pain in thumb or middle fingers with

forced palmar flexion for 90 seconds). Late findings consist of weakness of the abductor pollicis brevis and opponens pollicis muscles, and associated thenar eminence atrophy, or loss of sensation and two-point discrimination in median nerve sensory areas of the hand. An EMG may be helpful in confirming the diagnosis. It is important to rule out predisposing causes of carpal tunnel syndrome, such as pregnancy, diabetes, and hypothyroidism, treatment of which will often relieve the carpal tunnel symptoms.

Treatment for carpal tunnel syndrome includes use of a functional wrist splint (continuously or strictly at night), forearm conditioning focusing on the forearm flexors, and NSAIDs or occasional corticosteroid injection around the tendons. Surgical decompression should be considered if symptoms persist and EMG demonstrates evidence of median nerve injury.

DeQuervain's Tenosynovitis

Inflammation of the first dorsal compartment of the wrist containing the extensor pollicis brevis and abductor pollicis longus tendons causes this syndrome. This condition usually results from an overuse of the thumb for some particular activity that the patient is often able to identify.

On physical examination, the patient will have tenderness at and just proximal to the radial styloid. Swelling and crepitus of the first dorsal compartment is occasionally palpable. If the hand is ulnarly deviated with the patient's affected thumb tucked inside the other fingers, pain will often be elicited in the dorsal tendons where they pass over the distal radius (positive Finkelstein's test).

Treatment of DeQuervain's tenosynovitis includes thumb spica splinting for at least 1 week, ice, and NSAIDs. Phonophoresis (use of ultrasound to drive a corticosteroid across the skin), iontophoresis, or an occasional corticosteroid injection into the tendon sheath can also be of benefit. A stretching and strengthening program will improve conditioning of these muscles. Specific activity avoidance should be performed until strength improves and symptoms have significantly diminished. Surgical correction is rarely necessary.

Of note, any radial sided wrist pain in the anterior snuff box over the scaphoid bone must be treated as a scaphoid fracture until proved otherwise, even if initial radiographs are unremarkable.

Finger Injuries

Distal Interphalangeal (DIP) Joint Injuries

Mallet Finger. Mallet finger results from an injury to the extensor mechanism of the finger. The mechanism of injury involves a hyperflexion of the DIP joint (e.g., a ball hitting the tip of an extended finger forcing it into hyperflexion). This injury can occur in any activity in which the finger is subject to "jamming."

On physical examination, there is an inability to extend the DIP joint. There may be a full loss of extension, or an inability to obtain the last 10 to 20 degrees of full extension. Pain is present over the dorsal aspect of the DIP joint. On radiographic evaluation, 20% to 30% of patients will show a bony avulsion from the dorsal proximal distal phalanx.

Therapy for a mallet finger involves continuous splinting of the DIP joint in full extension for 6 to 8 weeks. The PIP joint can be allowed to move freely. If an avulsion fracture is present and involves more than 25% of the joint surface, referral is warranted. Serial observation should continue after immobilization to make sure extension is maintained.

Jersey Finger. This injury results from an avulsion of the flexor digitorum profundus tendon. Once avulsed, the flexor tendon may become trapped at several points along its path or may be retracted all the way to the palm. The mechanism of injury involves a forced extension of the distal phalanx while in the act of flexion (e.g., athlete grabbing on to a jersey).

On physical examination, the patient will be unable to flex the isolated DIP joint. Hematoma formation is commonly visible along the entire flexor tendon sheath. Tenderness is present over the middle portion of the middle phalanx as well as at the point of tendon retraction. Radiographs may be unremarkable or show a small bony fragment caught at the retraction site.

Treatment involves surgical reattachment of the tendon, preferably performed within the first few days of injury, to avoid permanent loss of flexion of the DIP or late more intensive reconstructive surgery.

DIP Dislocation. Dislocations of the DIP joint are usually obvious. Any forceful blow or avulsion to the DIP joint can result in a DIP dislocation.

On physical examination, there will be a deformity (often lateralization of the joint) and tenderness over the DIP joint. Prior

to reduction, there will be an inability to flex or extend the joint. Radiographs will show the dislocation.

Therapy involves both gentle pushing and pulling to obtain reduction. The DIP is generally stable postreduction requiring no further immobilization.

Proximal Interphalangeal (PIP) Joint Injuries

Collateral Ligament Injury. Injuries to the collateral ligaments of the PIP are the most common finger injuries. The mechanism usually involves a valgus or varus stress causing a partial or complete tear of the ulnar or radial collateral ligament. There is often a dislocation that has spontaneously reduced.

On physical examination, there will be tenderness over the specific injury site. Most commonly, the tear is located distally at the insertion on the middle phalanx, or midportion of the ligament. On stress testing, a variable amount of laxity will be found, depending on the extent of injury. Stress testing should be performed both in extension and 20 to 30 degrees of flexion, and compared with the uninjured side. Radiographs may show a small fleck of bone on AP view.

Therapy involves simple buddy taping for 6 to 8 weeks if stable (not a complete tear). Referral should be considered for radial collateral tears of the index finger due to the stresses this finger must sustain.

PIP Dislocation. The type of dislocation (dorsal versus volar) is determined by the position of the middle phalanx relative to the proximal phalanx. Dorsal dislocations involving the volar plate are the most common PIP dislocation. Volar dislocations involve injury to the central slip. Therapy postreduction centers on the ligamentous injury.

Central Slip Tears. Rupture of the central slip of the extensor digitorum communis over the PIP joint causes the lateral bands of the extensor mechanism to migrate volarly, subsequently leading to an inability to extend the PIP and eventually flex the DIP.

The mechanism of injury usually involves a blow to the dorsum of the middle phalanx against a semiflexed finger.

On physical examination, there is point tenderness over the dorsal aspect of the proximal middle phalanx, and often collateral tenderness as well. The lack of extension of the middle phalanx may be minimal on initial examination, but progressively worsen over weeks, with tightening of the DIP joint in extension.

If there is no associated fracture, treatment consists of splinting the PIP in full extension. The DIP joint can remain open to allow free flexion. The extension splint should be worn continuously for 6 to 8 weeks followed by gradual flexion of the PIP. If left untreated or improperly treated, this injury can result in a boutonniere deformity (flexion contracture of the PIP and extension of the DIP).

Volar Plate Tear. Rupture of the distal portion of the volar plate from its attachment to the middle phalanx occurs from a hyperextension injury to the PIP joint. The loss of the volar stabilizing force results in a hyperextension deformity of the PIP. On physical examination, the effected PIP joint will demonstrate increased extension compared with the uninjured side. There will be pain and swelling at the PIP joint with maximal tenderness on the volar aspect. With active extension and flexion, the hyperextended PIP often "locks" in the extended position with an inability to initiate flexion. DIP motion will be normal.

Volar plate injuries are treated with splinting at 15 to 30 degrees flexion for 3 weeks followed by progressive motion with splinting (buddy taping). If untreated, this injury may progress to a hyperextension deformity with the PIP in permanent hyperextension, and the DIP pulled into flexion.

Metacarpal Phalangeal Joint Injuries to the Thumb

Ulnar Collateral Ligament Sprain (Skier's/Gamekeeper's Thumb). Forced lateral stress with the MCP joint in near full extension, or a fall on an outstretched hand with the thumb caught in a position of abduction (fall on hand holding a ski pole) can result in rupture of the ulnar collateral ligament.

On physical examination, the patient typically has tenderness over the ulnar aspect of the first MCP joint and extreme pain with abduction stress. If there is more than 15-degree angulation with abduction stress occurs, compared with the opposite side, or absolute angulation of more than 35 degrees, it is considered a complete rupture. Radiographs will occasionally show an avulsion fracture from the proximal phalanx. If the adductor aponeurosis is caught between the torn collateral ligament (Stener lesion), adequate healing by conservative casting is less successful.

Therapy for incomplete ruptures involves thumb spica casting for 3 weeks followed by thumb spica removable splinting for

3 more weeks. If there is a displaced avulsion fracture >2 mm, or a complete rupture of the ligament, referral is warranted. Rehabilitation during and after the splinting stages includes active motion and alleviating any web space contracture.

Common Fractures of the Upper Extremity

Clavicle Fracture

Approximately 80% of clavicle fractures involve the middle third of the clavicle; thus, the focus of this section.

The mechanism of injury usually involves a fall on an outstretched arm, or to the lateral "point" of the shoulder. Less commonly, fracture results from a direct blow to the clavicle.

There is often a visible and palpable deformity, with marked swelling, ecchymosis, and pain, often radiating to the trapezius muscle. Though findings are rarely encountered, the patient should be examined for neurovascular compromise and for pneumothorax.

The degree of inferior displacement of the clavicular disruption can best be evaluated on the oblique view. A careful evaluation of the radiographs should also be performed to rule out an associated scapular fracture or pneumothorax.

The great majority of clavicle fractures can be treated conservatively with a sling. Often a figure of eight sling is used to draw the shoulders up and back to pull the clavicle back into alignment. Indications for referral for operative management include any sign of neurovascular compromise, interposition of soft tissue between the fracture fragments, or electively for severe uncontrollable deformity.

Fractures of the Humerus

Fractures and dislocations of the shoulder are classified by the number of parts displaced more than 1 cm or angulated more than 45 degrees from the other fragments. These include the anatomic and surgical necks or tuberosities. The proximal humerus is the site of 4% to 5% of all fractures, increasing in incidence with age and osteoporosis. Approximately 85% are not displaced or minimally so and can be treated by sling and range of motion exercises starting by 7 to 10 days postinjury. Others fall into the categories of 2- to 4-part fractures and generally require open reduction and internal fixation.

Humeral shaft fractures, if closed and uncomplicated by nerve or vascular injury, may virtually always be managed by hanging cast with the elbow flexed 90 degrees. Complicated fractures require such measures as U-shaped coaptation splint, abduction humeral splinting, skeletal traction, external fixation, open reduction, and shoulder spica.

Supracondylar fractures are to be greatly respected for the possibilities of entrapment of the medial nerve and/or brachial artery. While many can be managed by splint with the elbow flexed, observing closely the palpability of the radial pulse, most primary-care physicians would prefer to consult an orthopedist.

Medial and lateral condylar fractures are classified as Milch 1 and 2. For the lateral condyle, this depends on whether the fracture involves part or all the condyle and the degree to which the radiocapitellar joint is involved. Regarding the medial condyle, Milch 1 leaves enough trochlear ridge for stability; Milch 2 results in loss of the lateral trochlear ridge. Only the Milch 1 fracture of the medial condyle may sometimes be treated by closed reduction and immobilization without orthopedic fixation.

Fractures of the Radius

The radial head fracture is one of many that may be incurred from a fall onto the outstretched hand and it may be a complication of elbow dislocation. A diagnostic sign is the lucency seen on the lateral x-ray view called "the fat pad sign," whereby periosteal hemorrhage displaces the fat pad away from the volar aspect of the distal humerus. The chief complication is avascular necrosis of the radial head. Nondisplaced fractures can usually be treated with immobilization and early motion exercise. Fractures with partial head involvement or that involve the articular surface often require consultation, open reduction, and internal fixation.

The distal radius fractures occur with falls onto the outstretched hand, characterized by volar angulation (Colles) and less frequently, the reverse Colles with dorsal angulation (Smith fracture). Extra-articular nondisplaced fractures can be managed by immobilization for 6 to 8 weeks until healing occurs. Displaced fractures and fracture dislocations must be treated by closed reduction or external fixation with pins. The intra-articular fracture with dislocation of both the carpus and the distal ra-

lius is called the Barton fracture, most often managed by open reduction and internal fixation.

Scaphoid (Carponavicular) Fracture

This is yet another injury usually caused by falling onto the outstretched hand. The “boat-shaped” carpal bone situated on the radial side of the proximal carpal row, when fractured, often results in fewer symptoms acutely than may occur long term, if the diagnosis is missed. The arterial supply enters only at the distal end of the bone so that immobilization is crucial in order to re-establish vascularity. Twenty percent of fractures involve the proximal third, and, if not immobilized, 100% of these will undergo avascular necrosis. This fracture should be immobilized for 12 to 20 weeks. The middle third is fractured in 70% of cases, requiring immobilization for 6 to 12 weeks; and the distal third, involved in 10% of scaphoid fractures, should be immobilized for 4 to 8 weeks. To make the diagnosis, x-rays should include a PA film, and poly-tomography is very effective. Finally, bone scan 72 hours after the injury is 100% sensitive. For nondisplaced fractures (<2 mm in the fracture line), 95% will heal if immobilized by a short arm cast with the wrist at 10% flexion and radial deviation. In the event of displaced or other complication, open reduction and internal fixation are indicated.

Metacarpal (MC) Fractures

Most common are the “boxer’s” fractures of the fourth and fifth MCs, typically suffered in untrained fist fighting. These are less likely to be displaced than are their counterparts involving the second and third (index and long) finger MCs, which are more common in trained boxers. The fourth and fifth MCs are more likely, however, to be rotated. If treated closed, rotation is avoided by aligning the digits with 45 degrees flexion at the MCP and PIP joints and/or taping the fractured digit to the next finger during immobilization. This is supported by a gutter splint or short arm cast for 4 to 6 weeks. There is often ventral angulation in healing that is acceptable up to 30 degrees with informed consent, which can be avoided by internal fixation.

Long spiral fractures do not tend to rotate but require internal fixation to avoid nonunion. Shortening is common, of which 5 mm is tolerated.

Fractures of Phalanges of the Hand

Direct blows result in transverse fractures while twisting injuries tend to cause spiral fractures. Proximal phalanges are the most frequently fractured. They tend to exhibit volar angulation due to the actions of the interossei muscles while the distal fragment is pulled into extension by the central slip of the flexor tendon. These are usually reduced closed with external fixation, while oblique and spiral fractures require internal fixation. The best position of immobilization is 70 degrees flexion at the MCP joint and near, but not complete extension at the IP joints. Middle phalanges are much less frequently fractured. The most frequent complication is malrotation, seen most easily with the fingers in flexion, remembering that the fourth and fifth digits normally converge to a single point while the first and second digits converge on a separate point 1 to 2 cm lateral to the former.

Distal interphalangeal joint intra-articular fractures often result in the mallet deformity, wherein a portion of the articular surface was avulsed by the extensor tendon in a hyperflexion injury. These require splinting in extension for 6 weeks. Internal fixation is called for when $>30\%$ of the articular surface is lost, especially when accompanied by subluxation of the joint.

Proximal interphalangeal joints are involved in dislocations and fracture dislocations through hyperextension injuries, which cause avulsion at the flexor tendon insertion of a portion of the volar plate. Type 3 fractures include dorsal dislocation and retraction of the middle phalanx. These are treated by immobilization in 30 degrees flexion for 2 to 3 weeks followed by reduction of the flexion 10 degrees per week until 6 weeks have passed. Unstable fractures, defined as involvement of $>40\%$ of an articular surface, require open reduction and internal fixation.

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Mechanical Problems of the Lower Extremities

R. Trent Sickles

Evaluation and management of musculoskeletal problems in the lower extremities require sound basic knowledge of the anatomy and general function of the muscles, tendons, and ligaments in order that a specific diagnosis can be made and thereby a definitive treatment plan developed. Improper or general diagnoses, such as “knee sprain,” do not allow for the development of specific rehabilitation recommendations and may lead to failure of our patients to improve. In addition, understanding of the basic principles of different mechanisms of injury and how these impact on the healing process helps the physician to outline a rehabilitation protocol that maximizes healing. Finally, it is important that physicians understand the impact that a particular injury has on lifestyle, occupation, activities of daily living, and recreation.

INJURIES TO THE HIP REGION

Hip pointers are contusions of the iliac crest, usually caused from a direct blow either from an external projectile such as a football helmet or from contact with an immovable object like the floor. Pain is localized to the area of trauma and is increased with rotation and lateral bending of the trunk. Ambulation can also cause pain in some people. Treatment is primarily symptomatic, consisting of ice to the area for 20 to 30 minutes 4 times a day in

conjunction with pain medication, usually NSAIDs. As pain permits, stretching activities for the trunk should be added. Patients may return to normal activity as soon as their symptoms allow. Athletes in contact sports should use appropriate protective equipment to prevent injury.

Meralgia paresthetica is caused from irritation of the lateral femoral cutaneous nerve. Injury can be caused either from a blow near the anterior superior iliac spine where the nerve surfaces or when a patient sits, usually when wearing tight pants or a belt that impinges on the nerve. Patients will usually complain of numbness or tingling in the area supplied by the nerve. A sensory examination will confirm the diagnosis. Treatment consists of changing attire or modification of activity to avoid pressure on the nerve. Symptoms nearly always resolve spontaneously with this approach.

INJURIES TO THE THIGH

Muscle strains to the quadricep, hamstring, and adductor muscles are commonly seen. Most often they follow an explosive activity such as sprinting but can be seen with chronic overuse as well. The patient will usually report the sudden onset of fairly severe pain usually associated with a running or jumping activity. They may also describe a tearing sensation in the injured muscle. Physical examination may reveal echymosis and swelling of the injured muscle. After the patient is observed for obvious signs of injury, active muscle function as well as range of motion at both the hip and knee should be evaluated. Muscle strains are divided into three groups. Grade 1 injuries have limited clinical findings and do not limit activities. Grade 2 injuries cause swelling and echymosis, limited range of motion, and decreased strength. Grade 3 injuries are defined as a complete tear of the muscle tendon unit. Treatment principles are the same regardless of which of these muscles is injured. Ice and compression with an elastic wrap along with rest are recommended for immediate treatment. Crutches or another walking aid should be used until the patient can walk pain free without a limp. Stretching of the injured muscle immediately following the injury may limit muscle shortening and should be included as well in rehabilitation. Use of physical modalities for decreasing symptoms include the use of heat, ice, and muscle stimulation. Strengthening activities can be added to the rehabilitation program as soon as motion is nearly normal.

and pain permits. Before attempting strenuous athletic activity, controlled sport or activity-specific drills should be performed to be certain that symptoms do not recur.

INJURIES TO THE KNEE

Knee pain is one of the more common presenting musculoskeletal complaints. A thorough history can help in limiting diagnostic possibilities.

Anterior knee pain is usually associated with overuse, frequently running and jumping activity. The most common diagnoses include patellofemoral tracking problems or instability with subluxation or dislocation, patellar tendonitis, prepatellar bursitis, and in adolescents, Osgood-Schlatter's disease (tibial tubercle tendonitis).

Patellofemoral Instability

Patellofemoral instability is often associated with anatomic "risk factors." These include femoral anteversion, genu valgum (knock-kneed individuals), external tibial torsion, patella alta, and weakness of the vastus medialis obliquus muscle. History reveals insidious onset of symptoms that are frequently bilateral. Pain is usually increased by activity that causes knee flexion. Patients classically complain of pain after sitting with their knees flexed (theatre sign) and with stair climbing. Patients with subluxation or dislocation may have the ability to sense when the patella slips in and out of place. Physical examination begins with observation for the above risk factors. Carefully palpate anterior knee structures looking for evidence of effusion. Significant effusion can be associated with dislocation injuries, which can usually be differentiated from other tracking problems from the history. Observation of patellar tracking throughout the full range of motion may show evidence of lateral tracking and instability. Painful crepitation with patellar compression is consistent with this diagnosis. Evaluation of laxity at the quadriceps insertion containing the patella by firmly grasping the patella and moving it medially and laterally may also be helpful. With the knee flexed at 20 degrees, the patella should displace less than 50 percent of its width. Apprehension associated with lateral motion of the patella suggests patellar subluxation.

Treatment of patellofemoral pain associated with the above diagnoses can usually be managed with nonoperative therapy.

The use of NSAIDs to relieve pain is appropriate. Icing to prevent inflammation and decrease symptoms, especially after activity, is very effective. The mainstay of treatment involves improving flexibility of the quadricep and hamstring muscles, and strengthening the quadricep muscles, primarily the vastus medialis obliquus. This is generally accomplished with straight leg raising exercises, and extension exercises through a painless arc, usually the terminal portion of extension. Advanced strengthening exercises can be added as strength improves and pain permits. Taping or bracing to attempt to stabilize the patella can be beneficial in some individuals. A neoprene knee sleeve using a lateral buttress is the most commonly used brace. When patients comply with nonoperative therapy and symptoms persist for a minimum of 6 months, referral for surgical treatment should be considered.

Prepatellar Bursitis

Prepatellar bursitis is another cause for anterior knee pain. The history often is a blow to the anterior aspect of the knee, although repetitive micro trauma can also precipitate symptoms. Physical examination reveals swelling of the knee anterior to the patella, not to be confused with a joint effusion. Treatment consists of ice, compression, and NSAIDs to control pain. When this fails, drainage followed by compression, or even surgical excision of the bursa may need to be considered.

Anterior Cruciate Cartilages

A tear of the anterior cruciate ligament (ACL) is one of the more serious knee injuries and has significant implications for future prognosis, especially in physically active individuals. This ligament prevents anterior translation of the tibia on the femoral condyles. When it is torn, patients usually will have laxity and are at risk for additional injuries, especially cartilage tears. ACL injuries are usually noncontact. The patient will frequently report that it occurred when changing direction either horizontally or vertically. An audible pop is often heard followed by immediate pain and rapid swelling of the knee. Patients will report that they were unable to continue any activity and will often go to emergency departments for evaluation.

The physical examination varies depending on when the patient is seen. Immediately after the injury laxity may be seen. This

is best tested by a Lachman test, performed by flexing the knee at 20 to 30 degrees, stabilizing the femur with one hand and the proximal calf with the other. By pulling the tibia directly anteriorly, laxity can usually be found. When the ACL is intact and a Lachman test is performed, there is an abrupt halt to anterior translation. When the ACL is torn, there is not a sharp endpoint to this maneuver. After several hours, examination is much more difficult. The knee will usually have a large effusion. Range of motion is severely limited by swelling and pain. Ligamentous laxity is difficult if not impossible to test for because of the swelling and pain. X-rays should be obtained to rule out associated fractures. Initial management includes ice, compression, and nonweight bearing with crutches. A knee immobilizer can be used for comfort if desired. Pain medication is appropriate to control pain symptoms. Mild narcotics may be needed for a few days.

Follow-up evaluation after pain and swelling have diminished is necessary to confirm the diagnosis and recommend appropriate follow-up care. This is best done 7 to 10 days after the injury. Physical examination usually will reveal a joint effusion although less than on initial presentation. Motion will still be less than normal. Positive Lachman test and anterior drawer tests are the hallmarks of the diagnosis. Other injuries such as torn menisci and medial and lateral collateral ligaments often occur in conjunction with a torn ACL.

Long-term treatment for a torn ACL varies depending on each patient. For young (≤ 40 years), physically active patients, surgical reconstruction of the ligament should be strongly considered. Laxity and chronic instability associated with this injury markedly increase the risk for recurrent injuries and the development of premature arthritis. Reconstruction of the ligament with various types of grafts is felt to diminish these risks. In older or more sedentary individuals, nonoperative treatment may be more appropriate. This consists of aggressive physical therapy to strengthen knee flexion and extension. Bracing, usually with a custom-fit brace, can also be used to try and eliminate symptoms of instability. Patients who report episodes of giving way or other symptoms of instability are more likely to have problems in the future.

Medial and Lateral Collateral Ligaments

Sprains of the medial (MCL) and lateral (LCL) collateral ligaments usually occur as the result of a blow to the knee with the foot

fixed to the ground. The resulting varus or valgus stress to the knee results in tearing of the collateral ligament opposite the blow. Because a blow to the outside of the knee is more likely, tears of the MCL are more common. These injuries can occur in isolation or in combination with other knee injuries. Physical findings associated with isolated injuries include pain to palpation over the area of the tear and laxity. Laxity should be tested with the knee flexed at 20 to 30 degrees and in full extension. With the knee flexed posterior, capsular structures are relaxed. Valgus stress with the knee flexed tests for a tear of the MCL. Varus stress tests for a tear of the LCL. With the knee in full extension, posterior capsular structures are tight and become secondary stabilizers for varus and valgus stress. If laxity is present with the knee straight, the posterior capsule must be torn in addition to the collateral ligament. This a more severe injury and is more likely to require surgical intervention. Collateral ligament injuries are graded based on the degree of opening with varus or valgus stress. Comparison should always be made with the uninjured side to determine the amount of physiologic opening that is normal for the patient. Grade 1 sprains have 0 to 5 mm of opening; grade 2 sprains 5 to 10 mm of opening; grade 3 sprains greater than 10 mm of opening. As with ACL testing, the quality of the endpoint may be helpful in assessing the severity of the injury, with softer or absent endpoint being associated with more severe injuries.

Treatment of collateral ligament sprains that are isolated can usually be managed nonoperatively. For grade 1 and 2 sprains, weight bearing can be allowed as tolerated. Grade 3 sprains will usually require the use of crutches. The use of a brace to protect the knee from varus and valgus stress may be indicated for more severe injuries or to protect the knee in athletes who wish to return to activity. As with other injuries, the use of ice, compression, relative rest, and NSAIDs for pain relief are beneficial. Early motion exercises and strengthening as soon as tolerated are associated with a faster return to activity. Immobilization is unnecessary unless needed for a few days for pain control. Grade 3 sprains that are associated with other injuries such as ACL tears may require surgical intervention.

The Meniscal Cartilages

Tears of the menisci occur secondary to compression and shearing forces associated with activity. The history is usually one in

which the foot is planted and a twisting or shearing force is applied to the knee. Pain is immediate but not always enough that activity is stopped. The patient may report a pop or tearing sensation. Unlike ACL tears, in which swelling occurs within the first few hours, swelling associated with meniscal tears occurs later and may not be seen until the next day. The classic triad of symptoms reported with meniscal tears is swelling, locking, and giving way. Locking is caused when a piece of torn cartilage is displaced from its normal position and physically blocks motion of the knee. Giving out is caused when the meniscus is displaced and stimulation of the nerve supplying the meniscus causes a reflex "turning off" of the muscles, which causes the knee to buckle.

Treatment of meniscal tears is initially symptomatic. Ice, compression, and elevation are beneficial. Weight bearing is allowed as tolerated, although crutches may be necessary initially. Most meniscal tears require surgical treatment. Arthroscopic knee surgery has dramatically decreased the morbidity associated with meniscal surgery. On most occasions partial meniscectomy to remove the tear is the surgery performed, although meniscal repair can be attempted if the tear is small and peripherally located in the vascular area of the meniscus.

INJURIES TO THE LOWER LEG

Shin splints describes a syndrome of pain in the anterior to posterior-medial aspect of the lower leg. It is a nonspecific diagnosis, and treatment can be managed better when a specific diagnosis can be made. Medial tibial stress syndrome describes pain along the posterior medial border of the tibia. Onset of symptoms frequently occurs following periods of relative inactivity or at the beginning of a running program. Pain is brought on during activity and generally persists after activity, sometimes for several hours. Risk factors include rapid growth, especially during adolescence, anatomic factors such as pes planus, and mechanical problems such as hyperpronation. It is important to differentiate shin splints from tibial stress fracture. While the history can be similar, symptoms from stress fracture are usually more consistent and more severe. Physical examination reveals diffuse tenderness along the posterior medial aspect of the tibia usually near the middle and distal third of the tibia with medial tibial stress syndrome. Stress fracture should be considered in the differential diagnosis, to be discussed.

Treatment of *medial tibial stress syndrome* is managed by limiting activities that exacerbate symptoms. Since symptoms usually occur with either increases in training intensity or with changes in training technique, a decrease in intensity followed by a gradual increase to the desired level of intensity will usually limit symptoms. Icing after activity and use of NSAIDs also help to limit symptoms. Arch taping, shoe inserts, or orthotics may be beneficial for some athletes, especially if biomechanical problems that can be corrected are present.

Tibial stress fractures are often initially felt to be “shin splints.” Patients will frequently have a several-week history of symptoms of lower leg pain exacerbated with activity that they have been treating with episodic rest expecting their symptoms to abate. The classic history is that symptoms begin within a week or two of a change in training, usually a dramatic increase in mileage or intensity. Symptoms initially occur after the onset of activity and become progressively worse if activity persists. Running pain is worst during the foot strike phase of the gait. As time progresses symptoms will occur with decreasing levels of activity; for example, with walking and ultimately with rest.

Physical examination may reveal localized pain to palpation along the tibia over the fracture site. A forceful blow to the heel or placing a tuning fork over the suspected fracture can also cause pain at the fracture. X-rays are beneficial only when they show definite evidence of a fracture. Advanced fractures can have significant cortical thickening that is easily palpable and readily evidenced on x-ray. A horizontal line seen on x-ray through the area of cortical thickening (the “dreaded black line”) is a poor prognostic sign and referral to an orthopedic specialist is indicated. Normal x-rays do not definitely rule out stress fractures, and when the history and examination suggest this diagnosis, a bone scan should be ordered before a treatment plan is developed.

Management of tibial stress fractures, especially if diagnosed early, can consist of simple elimination of running and jumping activity. Weight bearing can be allowed as long as it does not cause pain or crutches can be used as necessary. Conditioning activity such as swimming can be performed to maintain fitness. Biking and a stair climbing machine can be added after 2 to 4 weeks as symptoms improve. No running or jumping should be permitted for at least 6 weeks. A menstrual and dietary history is important in women diagnosed with stress fracture. Amenorrhea is a significant risk factor for stress fracture, and adequate dietary

calcium and consideration for hormonal treatment are an important part of therapy.

Gastrocnemius Tears

Acute strain of the gastrocnemius muscle presents with a history of acute pain, usually in the proximal postero-medial aspect of the calf. Patients frequently feel as if they were struck with an object such as a tennis or racquetball. Swelling and echymosis may be present depending on the severity of the injury. Grading of muscle strains is described earlier in this chapter. Physical examination should include testing for muscle range of motion and strength. Passive ankle dorsiflexion and active plantarflexion increase symptoms. Patients with significant tears are unable to perform a toe raise standing on their injured legs. This is an excellent functional test that can be used to determine if an athlete is ready to return to sport-specific training before resuming competition. Palpation of the injury site is painful, and a palpable defect may be present with more severe injuries. Echymosis can be present at the injury site but frequently is seen distally as far as the heel.

Treatment is symptomatic, with early range of motion followed by strengthening. Crutches can be used for relief of symptoms until ambulation is possible without pain or a limp. Ice and NSAIDs are also helpful early. Once symptoms permit, gradual return to activity can be allowed.

Achilles Tendon

Common injuries to the achilles tendon include acute strains, and tendonitis, which is usually more insidious in onset. Acute strains range from mild injuries to complete tears. History is generally straight forward, with the abrupt onset of pain in the posterior aspect of the heel or distal leg. With achilles tendon rupture, severe pain and swelling are usually present. Swelling may make palpation of a defect in the tendon impossible, and for this reason rupture of the tendon may be missed. Performance of a Thompson test prevents this missed diagnosis. To perform the test, have the patient lie supine on his/her abdomen with the knee flexed at 90 degrees. Grasp the midportion of the calf and gently squeeze. If the achilles tendon is intact, the foot should plantar flex as the calf is squeezed. A positive test, where there is no plantar flexion, is highly suggestive of achilles tendon rupture. This problem should be referred to a specialist for possible

surgical repair, versus prolonged casting with the foot in plantar flexion. Less severe strains of the achilles tendon can be managed with ice, NSAIDs, and limited activity. Crutches or a walking boot may be needed to control symptoms initially with grade 2 strains. Early range of motion followed by strengthening before return to activity is warranted.

Achilles tendonitis generally presents with a several-week history of posterior heel pain that worsens with activity. It may be precipitated by a change in training such as increased hill running or following a specific activity such as running a marathon. In most cases there is no history of a specific precipitating acute event. Pain improves with rest but returns as soon as activity resumes. The patient may or may not notice swelling in the area of the tendon.

Physical examination reveals tight heel cords that may be painful with stretching. Active plantar flexion against resistance is usually painful. Pain to palpation is present in the distal calf most frequently at or near the enthesis. In patients with chronic symptoms, palpable thickening or nodularity of the achilles tendon may be present.

Treatment includes ice, NSAIDs, and aggressive stretching of the posterior leg. Heel lifts may be beneficial in reducing symptoms temporarily by shortening the muscle-tendon unit with everyday activity, but they must be used in conjunction with a stretching program to prevent even further tightening of the heel cords. Once symptoms have subsided, a slow return to activity can be attempted. Symptoms can be frustratingly slow to completely dissipate, and patients should be cautioned regarding too rapid a return to intense levels of exercise.

INJURIES TO THE ANKLE

Ankle sprains are one of the most common injuries seen by primary-care physicians. Careful evaluation will assure that uncommon complicating conditions or other diagnoses that mimic ankle sprains initially but may have a poorer prognosis are not overlooked.

Inversion and plantar flexion causing a lateral ankle sprain is the most common mechanism of injury. The anterior talo-fibular ligament is the most commonly injured lateral ligament. The calcaneo-fibular and posterior talo-fibular ligaments are torn or injured with more severe sprains. The patient was usually running on an uneven surface or misstepped unexpectedly. Pain is

immediate, and swelling can occur quickly. Minor or grade 1 sprains are often “walked off” by athletes and are rarely seen in physicians’ offices or emergency departments. Moderate or grade 2 sprains will usually have significant swelling over the lateral ankle within several hours. The swelling may spread to the medial and anterior aspects of the ankle depending on the severity of the sprain and on initial treatment. Tenderness to palpation occurs over the lateral ankle, and a positive anterior drawer test may be present. This is performed by stabilizing the tibia and grasping the posterior calcaneus with the opposite hand. The examiner then pulls directly forward on the calcaneus, and anterior displacement of the talus on the tibia is a positive test. This can be compared with the uninjured side. Initial pain and swelling may limit the usefulness of this test. X-rays should be obtained to rule out fractures. The proximal head of the fifth metatarsal should be palpated and x-rays obtained to rule out a fracture of this bone when any pain is present on examination. Examination of the proximal fibula is also important to assess for a possible Maisonneuve fracture. While these associated fractures are not common, they are missed because of failure to thoroughly evaluate a patient with “just a sprain.” Third-degree sprains involve complete tearing of all three lateral ligaments and are associated with instability. Stress x-rays reveal tilt and significant anterior displacement of the talus relative to the tibia. Despite this instability, nonoperative treatment is still possible. Referral to a specialist should be considered for third-degree sprains because of the risk of symptoms from chronic instability.

Eversion sprains, while less common, have the potential to cause more severe symptoms and are generally more difficult from which to recover. The history is usually that the foot was planted and a sudden twisting motion caused forced eversion and rotation of the ankle. In addition to injuring the deltoid ligament medially, the rotational forces can also injure the tibiofibular ligaments and the interosseus membrane. This has the potential to cause instability from widening of the ankle mortise. X-rays should be obtained and careful attention paid to the mortise. Fractures are associated with eversion more frequently than with inversion injuries. When in doubt, referral for possible surgical stabilization is warranted. When the mortise is intact and no fracture is present, nonsurgical management is appropriate. Many patients will benefit from 2 weeks in a walking ankle-foot orthosis or

a walking cast if their injuries are extremely painful. Alternatively, nonweight bearing on crutches followed by partial weight bearing is also beneficial in reducing pain symptoms. Early range of motion and other physical therapy is warranted to try to prevent prolonged symptoms. Eversion sprains commonly take 6 weeks or longer to rehabilitate. Persistent pain should be re-evaluated for other diagnoses or instability.

Fractures associated with ankle injuries include small avulsion fractures, distal and proximal fibular fractures, fractures of the posterior process of the calcaneus, and of the anterior process of the calcaneus fractures. More complex fractures involving the ankle joint can occur but are beyond the scope of this text and will generally not be seen initially in a family physician's office because of their obvious severity. Small avulsion fractures of the medial and lateral malleolus are frequently seen and represent small flakes of bone that are avulsed as the tendon tears. These can generally be managed the same as a comparable sprain.

Fractures of the distal fibula can occur as well. When these are nondisplaced and the ankle mortise is maintained, they can be treated with either a walking ankle-foot orthosis or a semirigid stirrup type ankle orthosis, depending on the severity of symptoms. Crutches can be used for comfort. Range of motion activity should be begun as soon as symptoms permit. Progression of activity can occur while wearing a stirrup orthosis usually beginning with biking or swimming and progressing back to running activity over about 6 weeks.

Fractures of the posterior process of the talus can easily be missed. The mechanism of injury is usually hyperplantar flexion, and pain is present in the posterior aspect of the ankle. These may be mistaken for achilles tendonitis unless carefully evaluated. The patient will complain of pain with plantar flexion of the foot. Tenderness to palpation is present over the posterior process of the talus, which is located deep to the distal portion of the achilles tendon. A positive bounce test is elicited by rapidly plantar flexing the ankle, causing pain posteriorly as well. The fracture can be seen on the lateral x-ray. An os-trigonum, which is an ununited posterior process, may be mistaken for an acute fracture. Fractures will usually have sharp, irregular borders, whereas an os-trigonum will usually have smooth, rounded edges. Posterior process fractures should be treated with immobilization for 2 to 4 weeks followed by rehabilitation exercises and a gradual re-

turn to activity. Most injuries of the posterior process should be healed within 6 weeks and persistent pain should be evaluated for a possible nonunion.

Fractures of the anterior process of the calcaneus can mimic an ankle sprain. The fracture is most easily identified on a lateral oblique x-ray. When identified early, immobilization in a short leg cast for 4 to 6 weeks is the treatment of choice. Old fractures may require surgery.

INJURIES TO THE FOOT

Plantar fasciitis is one of the most common painful problems seen by family physicians. Symptoms are usually insidious in onset, with most pain being localized to the medial plantar surface of the heel usually just distal to the fat pad. Pain is usually worst first thing on arising and improves with activity, although prolonged activity can increase symptoms. Patients will also complain of increased symptoms after periods of sitting or resting. Physical examination will reveal tenderness to palpation over the medial plantar surface of the heel. Pain may be present with forced dorsiflexion of the ankle, especially if the toes are extended. Biomechanical problems such as pes planus and evidence of excessive pronation increase the likelihood of plantar fasciitis. Treatment includes icing, NSAIDs, and stretching of the plantar fascia and heel cords. Heel lifts or heel cups can provide temporary relief. For recalcitrant cases, use of the physical therapy modalities ultrasound and iontophoresis may provide some relief. Injection of corticosteroids into the insertion of the plantar fascia on the os calcis can also provide benefit. Risks of injection include fat pad atrophy if the injection is inadvertently placed in the fat pad of the heel, infection, and rupture of the plantar fascia. Rupture will generally cause abrupt increase in pain and swelling often with a history of a pop. Rupture of the plantar fascia can be managed similarly to plantar fasciitis and generally carries a good prognosis. Orthotics can be considered when contributory biomechanical problems are present.

Stress fractures of the foot bones are relatively common occurrences with runners. Symptoms are usually insidious in onset but can occur during a specific event such as a marathon. The classic history is one in which a change has occurred in training like a sudden increase in distance, intensity, or a change in equipment or running surface. The patient will usually complain of

pain during the foot strike portion of the gait. Symptoms are reproducible, often occurring at the same point during a run each day. Examination will show tenderness over the stress fracture site. Localized swelling may also be present. X-rays may reveal periosteal elevation or cortical thickening but may be completely normal. When clinical signs and symptoms are present, a bone scan should be considered for definitive diagnosis. Alternatively, an assumed diagnosis of stress fracture can be made and treatment initiated appropriately. Stress fractures of the second, third, and fourth metatarsal bones are stable injuries that can be managed with a stiff shoe, such as a cast shoe and limitation of activities for 4 to 6 weeks. Biking, swimming, or other nonrunning activities can be performed to maintain conditioning. Running activity can be resumed when clinical symptoms are gone and a minimum of 4 weeks has passed since treatment was begun.

Stress fractures of the fifth metatarsal may not be stable and should be managed differently from second, third, and fourth metatarsal fractures. Referral to an orthopedic surgeon should be considered. Definite diagnosis and localization of the fracture site for fifth metatarsal stress fractures are important for determining treatment plans and prognosis. Metaphyseal fractures carry a high risk of complete fracture or nonunion and need to be managed aggressively either with a short leg cast, nonweight bearing for 6 weeks or surgically with an intramedullary compression screw. A surgical approach generally allows a quicker return to activity with less risk of nonunion but carries the obvious risks of surgery. Nondisplaced fractures of the styloid process of the fifth metatarsal carry a better prognosis and can be managed with an ankle foot orthosis or short leg walking cast for 4 to 6 weeks.

Stress fractures of the tarsal navicular bone or of the cuboid bones are uncommon injuries. These often do not respond well to treatment and should be referred to an orthopedic or sports medicine specialist for treatment.

Hyperextension injuries of the great toe are often referred to as turf toe. Hyperextension causes a sprain of the plantar capsular ligaments of the first tarsal metatarsal joint. Treatment includes icing, NSAIDs, and rest. Return to activity is based on symptoms. Taping to prevent dorsiflexion of the great toe and modification of shoes to stiffen the forefoot are also beneficial. This is an injury that frequently will cause symptoms for several weeks, with implications for an athletic season.

Approach to the Patient with Rheumatic Disease

Lori B. Siegel and Eric P. Gall

EVALUATION OF THE PATIENT WITH RHEUMATIC DISEASE

The evaluation and diagnosis of patients with rheumatic complaints are dependent on a thorough and detailed history and physical examination (H&PE_x), which, despite the advances in laboratory and radiographic testing, remain the most valued tools. The chief complaint in rheumatic diseases may involve joint pain or may reflect more systemic problems. For reasons that will be reviewed in detail, any patient with a new rheumatic complaint requires inquiries regarding recent or concurrent illnesses, especially those of an infectious nature; constitutional symptoms such as fever, chills, weight loss and fatigue, and the type of progression of the articular complaints (e.g., intermittent, migratory, or additive).

TENDONITIS

Tendonitis is a general term used to describe any inflammatory condition associated with a tendon. These may be divided into tenosynovitis, intratendinous lesions, and tendon tear/rupture. Tenosynovitis is an acute or chronic paratendinous inflammation. Repetitive motion injuries of or microtrauma to the tendon causes local edema, decreased gliding of the tendon surfaces, and subsequent mechanical block. A good working knowledge of common bursal and tendon syndromes will aid in diagnosis (Table 25.1). A

Table 25.1.
Common overuse syndromes.

Syndrome	Area Involved
DeQuervain's tenosynovitis	Flexor pollicus longus
Trigger finger	Flexor tendons of the hands
Rotator cuff	Any of the rotator cuff tendons
Housemaid's/Carpenter's knee	Prepatellar bursa
Miner's shoulder	Subdeltoid/acromial bursa
Pump bumps	Retrocalcaneal bursa

thorough work-up and social history must be obtained. A septic process causing the tenosynovitis must be considered when preceded by a direct wound or a concurrent gonococcal infection. The PEx will reveal pain with motion, especially passive stretching. The positive range of motion (PROM) of the neighboring joint will remain full. Local edema, warmth, tenderness, and occasionally erythema may be present. The treatment for tenosynovitis entails cessation of the offending movement and a course of immobilization or splinting, until the inflammation subsides, not longer than 3 to 4 days. Local heat and NSAIDs are helpful. PROM exercise maintains muscle strength and normalizes biomechanics. If no infection exists, often a paratendinous injection of depot corticosteroids is valuable, avoiding injection into the tendon so as not to weaken and predispose it to rupture. Usually 10 to 20 mg of methylprednisolone acetate or triamcinolone acetonide (TA) mixed with 1% lidocaine is used. Such injections should not be given more than 3 to 4 times per year. Common types of tenosynovitis include flexor pollicus longus (DeQuervain's tenosynovitis), and trigger fingers, involving the flexor tendons of the hand.

Intratendinous lesions generally occur later in life as the vascularity diminishes. Microtrauma from repetitive movements or impingement syndromes set up the inflammatory response. During the reparative phase, calcium salts (hydroxyapatite) may be deposited. Common sites of intratendinous lesions are insertions at the lateral and medial condyles of the elbow, (tennis and golfer's elbow, respectively), bicipital tendonitis, and rotator cuff injuries. These lesions also respond to local measures with an emphasis on physical therapy.

Rotator cuff injuries comprise the spectrum from tendonitis to acute rupture. With a complete tear, the patient will be unable

to initiate and/or sustain abduction of the shoulder without the tell-tale shrug of assistance. The MRI is most valuable diagnostically. In the treatment of rotator cuff injuries, transient splinting is acceptable after the acute injury, but early physical therapy is essential to preserve range of motion. Intra-articular corticosteroids may help to alleviate the pain so that the patient may participate appropriately in physical therapy. If untreated or inappropriately treated, adhesions will form in the shoulder with ultimate adhesive capsulitis, which will require extensive physical therapy and even surgery. Large rotator cuff tears often require surgical intervention. Other common tendinous ruptures include the biceps, Achilles, quadriceps, and plantaris tendons.

BURSITIS

There are more than 260 bursae in the body, and bursitis is a frequent diagnosis of soft tissue rheumatism. Bursae facilitate motion and are present in areas where tendons and muscles move over bony prominences and may form in response to irritative stimuli. Bursitis may occur because of repetitive motion, overuse, or trauma and accompany rheumatoid arthritis and gout.

The H&PEx are the most useful tools in evaluating bursitis. Calcium deposits may be evident radiographically and often are indistinguishable from calcific tendonitis. The patient will have localized pain with occasional radiation into the involved limb. Swelling may or may not be present depending on the anatomic site. There may be erythema and warmth independent of infection. There will be pain with movement of the stressed motor unit and tenderness to palpation. PROM of the joint is full. Wounds, nearby cellulitis, or previous injection may indicate a septic bursa. Aspiration of the bursa is mandatory when infection is suspected, and the fluid should be Gram's stained and cultured. The most common organisms cultured are staphylococci and streptococci. Antibiotics should be administered based on clinical scenario and Gram's stain. Repeat aspiration may be indicated if the fluid reaccumulates.

For the nonseptic bursa, conservative therapy is often sufficient. Rest and immobilization of the affected area is permissible short term. Ice compresses and NSAIDs will also minimize the degree of inflammation and pain. For persistent or recurrent nonseptic bursal inflammation, aspiration with an intrabursal injection of corticosteroid may be helpful. The dose for this is 10 to

30 mg of TA or methylprednisolone acetate. Recalcitrant bursae that affect function may need surgery. Prepatellar bursitis is seen in many occupations in which a great deal of time is spent on the knees. While it may look exactly like a joint effusion, careful PEx will localize the edema to the prepatellar area. Miner's shoulder and pump bumps are bursal syndromes involving the subdeltoid/acromial and retrocalcaneal bursae, respectively. The olecranon bursa is commonly involved in patients with gout.

FIBROMYALGIA (FIBROSITIS)

The patient with fibromyalgia complains of overwhelming pain, fatigue, and extra-articular features. Once a careful H&PEx are completed, the diagnosis becomes more obvious.

The presentation is often that of hurting all over, both in and around all the joints. Reports of morning stiffness, achiness, and swelling of the joints and soft tissues are frequent. Associated complaints of irritable bowel syndrome, migraine or tension headaches, paresthesias in a nonanatomic distribution, and even severe dysmenorrhea are not unusual. Patients should be screened via H&PEx for any evidence of true connective tissue disease or endocrinopathy. The PEx is essentially normal and fails to confirm the perceived swelling. Nerve conduction studies do not confirm a neuropathy. Localized areas of exquisite tenderness around the joints called tender points are found. These tender points may coincide with classic areas of tendonitis, but the patient with fibromyalgia will have exquisite tenderness over a majority of sites without any history of overuse. The proposed criteria for fibromyalgia consist of severe widespread pain and at least 11 out of 18 specific tender points (Fig. 25.1).

Often there has been some antecedent traumatic event, either emotional or physical, which leads to disruptions in sleep patterns. Most patients will admit to poor quality sleep — either noncontinuous or continuous sleep that is not refreshing. Sleep studies have indeed shown decreased delta wave sleep, which is the deep restorative sleep. Normal controls have developed the tender points of fibromyalgia if their delta sleep was disturbed by an auditory stimulus (1).

Laboratory tests and radiographs are not revealing in fibromyalgia. Fibromyalgia may also accompany other longstanding illnesses that themselves may cause severe pain. In patients with known chronic disease who suddenly develop generalized or

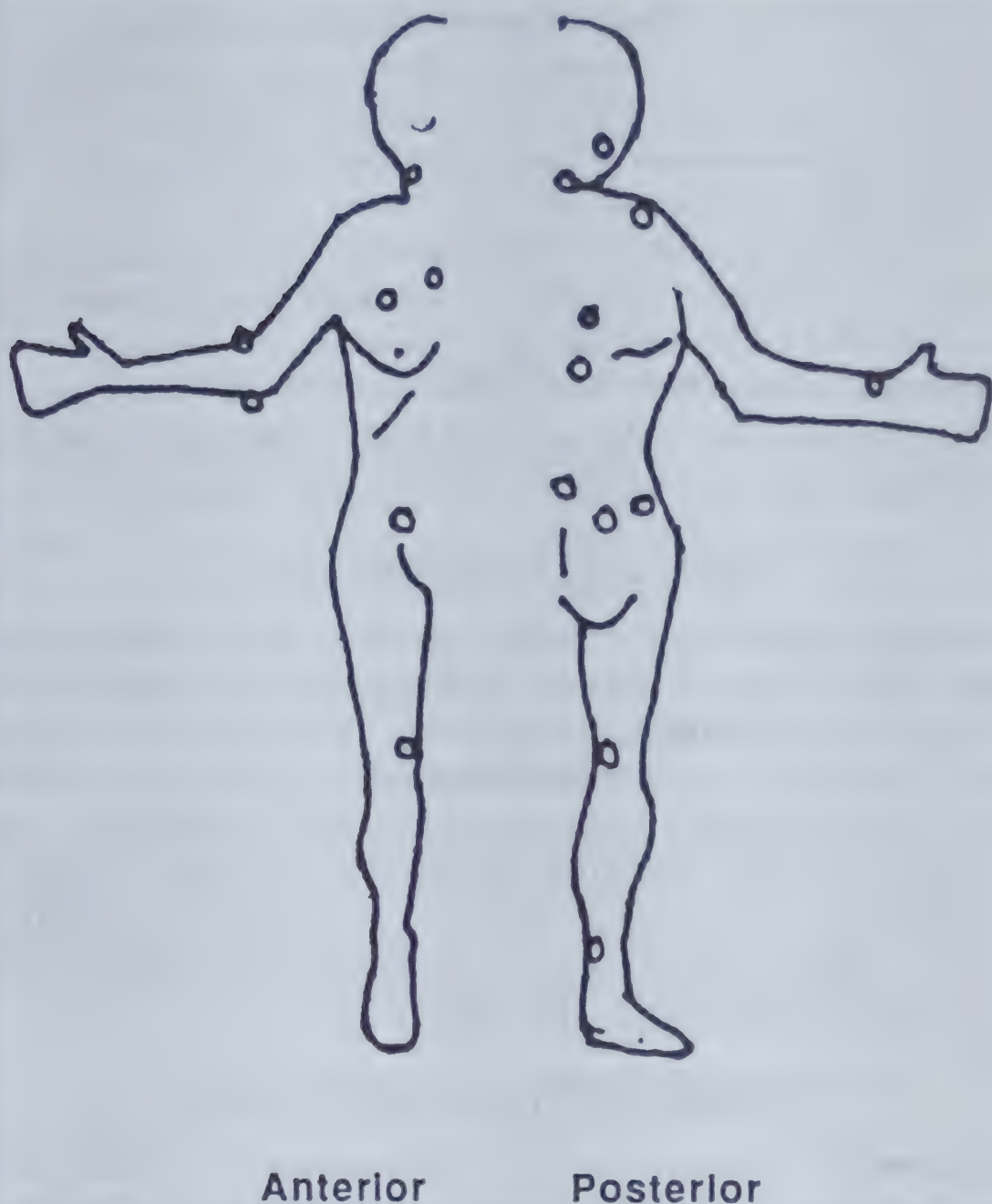


Figure 25.1. Tender points in fibromyalgia; anterior (left), posterior (right).

worsening pain and difficulty sleeping, secondary fibromyalgia needs be considered.

The treatment of fibromyalgia is reassurance and sleep restoration. Many patients have been told by multiple physicians that the pain was all psychologic. Fibromyalgia support groups are important. Restoration of sleep can be accomplished with use of low-dose amitriptyline (Elavil) (2), cyclobenzaprine (Flexeril) (3), and alprazolam (Xanax) (4) given at bedtime to control the sleep cycle. Treatment should be initiated at the lowest dosage possible and gradually increased over 2-week intervals until the sleep cycle improves or adverse effects are encountered. Patients should be cautioned regarding the anticholinergic

gic effects and initial drowsiness with these medications. The body adapts to the drowsiness, and the patient should be encouraged to stay with the program. Improvement may be slow, and a daily journal may be helpful to allow the patient to see the progress that is made.

NSAIDs are not helpful for fibromyalgia per se but may help alleviate any underlying pain due to osteoarthritis or tendonitis. Narcotics should be avoided because they affect the sleep cycle in a nonrestorative manner. Temptation to inject all of the tender points should be avoided since it may lead to dependence and does nothing to alter the underlying disorder. Exercise is important.

MYOFACIAL PAIN SYNDROMES

Localized nonarticular muscular pain is often termed myofascial pain. This is often in response to alterations in or poor posture during lifting or prolonged immobility. The pain and discomfort are limited to a specific region, remain localized and are unilateral. PEx may reveal a trigger point that when pressed may cause pain to radiate in a recognized distribution. Treatment for this is attention to proper muscle alignment and stretching with either heat or cold application. Often, patients respond to anesthetic or corticosteroid injection of the trigger point.

HYPERMOBILITY SYNDROMES (HMS)

Hypermobility of joints may occur as a feature of hereditary connective tissue disorder (CTD) such as Ehlers-Danlos, or Marfan's syndrome, but it is the "benign hypermobility syndrome" (BHMS) that causes most musculoskeletal complaints. These patients may present with overuse syndromes, traumatic lesions, and traction injuries involving tendons and ligaments. Joint instability or chronic arthritis with some synovitis is found. Individuals often present with arthralgias and myalgias with absence of clinical abnormality. Associated extra-articular features include hyperextensible skin, striae, mitral valve prolapse, and weakness of the abdominal wall resulting in abdominal and pelvic pain. Stress fractures are also common as a result of increased bone fragility. The diagnosis is based on the ability of the individual to perform a series of passive joint maneuvers such as hyperextension of the elbow or knee, apposition of thumb to the flexor aspect of the forearm, and passive dorsiflexion of the fifth MCP to 90 degrees,

and forward flexion of the trunk placing the hands flat on the floor with the knees extended.

The treatment of BHMS is primarily supportive with education and reassurance that the patient does not have a deforming or crippling disease. Conditions that aggravate the discomfort should be avoided, and stretching and muscle strengthening exercises may help stability.

THE PROBLEMS OF TRUE JOINT PAIN

If the PEx reveals limitation of PROM, then true articular pathology is considered although some arthritic processes allow full PROM. The next decision is the determination of whether the arthritis is inflammatory or noninflammatory. If the cardinal signs of inflammation are extremely mild or absent, then osteoarthritis is a likely diagnosis.

Osteoarthritis (OA)

OA is characterized by progressive loss of articular cartilage and subsequent reactive new bone formation. Women tend to have more severe disease, increased number of involved joints and an increased frequency of deformities; men have an earlier onset of symptomatic disease and a more prominent hip and spine pattern of involvement. OA may be asymptomatic for many years and present with pain, stiffness, crepitus, joint locking, or a gait disturbance. The pain is usually worse with activity and relieved with rest, but prolonged rest may incur stiffness. The stiffness associated with OA is shorter than with inflammatory conditions, lasting less than one-half hour. Prior history of trauma, be it physical injury or secondary to other joint diseases, predisposes the joint to OA.

Generalized OA primarily involves the spine, weight bearing joints, knees, hips, and metatarsophalangeal joints, sparing the ankle unless there has been antecedent injury. The carpo-metacarpal joints, proximal, and distal interphalangeal joints may also be involved. PEx may reveal pain on AROM and PROM with no synovial hypertrophy and bony enlargement at the joint margin. Crepitus, joint instability, and deformity may be noted. The laboratory tests, including sedimentation rate and synovial fluid analysis are without abnormalities. Radiographic findings of asymmetric joint space narrowing, subchondral new bone formation

(eburnation/sclerosis), and marginal spurs or osteophytes are diagnostic. The absence of erosions and osteoporosis is helpful in excluding underlying inflammatory diseases. Radiographs of the lower extremity should be taken with weight bearing views to accurately assess the degree of joint space narrowing.

The guidelines for the management of OA are directed at relieving pain, maintaining joint function, and halting progression. These are accomplished mainly by education, weight reduction, and trauma avoidance. Essential physical measures including scheduled rest periods, heat application, and active range of motion are essential. Acetaminophen is the first line of medical therapy and should be administered on a regular basis for maximum pain relief. If the patient fails a 2-week trial, then NSAIDs may be administered at low or analgesic doses. If inflammation is present, higher doses of NSAIDs may be indicated with close attention to increased frequency of side effects, especially in the older population. Nonacetylated salicylates may be associated with fewer gastrointestinal reactions. Topical analgesics and other nonnarcotic analgesics may be useful. Low-dose narcotics may be necessary for severe pain or in those patients for whom NSAIDs are contraindicated. Intra-articular injections of corticosteroids may be beneficial when used cautiously for acute flares of pain. Injections should be infrequent, especially in the weight bearing joints, since they may mask the pain and lead to activities that actually exacerbate the arthritis. Oral or parenteral corticosteroids play no role in the treatment of OA. Surgical treatment and joint replacement with perioperative physical therapy are indicated when the pain is severe and interferes with activities of daily living, despite medical therapy. Arthroscopy, arthroplasty, and osteotomy may be tailored as indicated for stability, mobility, and independence.

Erosive Osteoarthritis (EOA)

This is an inflammatory subcategory of OA that features articular cartilage erosion and osteophyte formation. EOA involves primarily the distal and proximal interphalangeal joints of the hands, the classic Heberden's and Bouchard's nodes, respectively. Severe deformity and ankylosis result, without pain or sometimes with severe pain and inflammation. NSAIDs in anti-inflammatory dosages are useful.

Inflammatory Arthritis

Inflammatory arthritis manifests the cardinal signs of warmth, erythema, tenderness, and swelling. Inflammatory conditions may also be associated with constitutional symptoms such as fatigue, malaise, alteration in weight, and fever. Stiffness upon awakening and with immobility is a feature of an inflammatory process that usually lasts longer than 30 minutes and improves with activity and movement. Synovial fluid analysis is the only definitive way to confirm an inflammatory process. Once an inflammatory arthropathy is established, the number and pattern of involved joints narrows the diagnostic possibilities.

Oligo-articular Inflammatory Arthritis

A careful PEx is necessary to determine the number of involved joints since patients may complain of only one or two joints among the several involved. If one joint is involved, it is termed mono-articular arthritis, and if three or fewer are involved, the adjectives oligo- or pauci-articular apply. The differential diagnostic possibilities are usually limited to infectious, crystalline, or traumatic arthritis. The key to establishing the diagnosis is synovial fluid aspiration and analysis. All three may present with leukocytosis and constitutional symptoms or present concurrently. Appropriate and efficient treatment therefore depends on history and synovial fluid analysis.

Septic Arthritis

This is a medical emergency. If not promptly diagnosed and treated, the joint destruction can lead to immobility, loss of function, and OA. Twenty percent of patients will present with more than one infected joint. Joints usually become infected secondary to hematogenous spread. Therefore, a search for the underlying source of infection is crucial. Occasionally a joint may become infected via contiguous spread of a cellulitis or osteomyelitis or as a result of direct implantation. Predisposing factors include bacteremia, underlying damaged joints, concurrent chronic illnesses such as diabetes, concurrent therapy with corticosteroids or other immunosuppressives, prosthetic joints, intravenous drug abuse, recent trauma, or intra-articular injection. Any joint can be affected. Hematologic findings are nonspecific at presentation, e.g.,

elevated sedimentation rate, with a leukocytosis in 50%. Synovial fluid should be sent for Grams stain, cultures, crystal analysis, glucose, and cell count. The synovial fluid of a septic joint will often reveal WBCs ranging between 20,000 and 50,000/cm³ or above with a predominance of neutrophils. The glucose is usually less than half that of the serum. Crystals can be found with a septic joint with coexistent crystalline disease. Grams stains guide therapy; they are positive, with staphylococci in 50% of the cases, Gram-negative bacilli in 10%, and gonococcal infections in 25%. Early radiographs reveal joint effusion, soft tissue swelling, edema of the fat pad, juxta-articular osteopenia, and in anaerobic infections, gas in the joint. If untreated, or not optimally treated, later radiographic changes include joint space narrowing, cartilaginous erosions, and subchondral bone destruction. Diffuse loss of bony cortex is a late sign.

The treatment of infectious arthritis requires intravenous antibiotics and removal of the septic fluid. Serial aspirations and joint lavage may be necessary to adequately drain the joint. Depending upon the rate of fluid reaccumulation, aspiration may be required up to 3 times daily. Some advocate the use of early arthroscopic joint debridement. The joint fluid is monitored by serial cell counts. "Adequate control" of the infection is defined as a significant decrease in the synovial white cell count within 48 hours and subsequent negative cultures. The antibiotic choice is determined by the historical clues regarding the causative agent and the result of the Grams stain and culture. A minimum of 1 to 2 weeks (often longer) of intravenous antibiotics is needed followed by oral antibiotics as needed. Intra-articular antibiotics are avoided since they cause a chemical synovitis. Surgical drainage is required when needle aspiration is not sufficient or there is inadequate drainage due to anatomic difficulties, loculated pus, and in children who refuse repeated aspirations. Passive range of motion and muscle strengthening exercises should begin as soon as the joint inflammation has subsided. Prolonged splinting should be avoided as joint fusion may recur.

Gonococcal (GC) arthritis is an interesting variant with two phases. The initial presentation is that of an arthritis dermatitis syndrome with fever or chills. Skin lesions develop on the fingers and toes that may be petechial, pustular, or hemorrhagic, usually healing within 4 to 5 days. An associated polyarthralgia without true synovitis occurs. The septic joint phase follows during which

patients are afebrile and have a monoarticular effusion. Culture yields are greater at this phase. The diagnosis of GC arthritis is confirmed by positive synovial, pharyngeal, urethral, or rectal cultures. One percent to three percent of GC infections are disseminated. Recurrent attacks indicate a possible terminal complement deficiency. Treatment for GC arthritis is high dose ceftriaxone.

Crystalline Arthropathies

The initial attack of gout or calcium pyrophosphate disease (pseudogout) may look like a septic joint with associated constitutional symptoms such as fever, tachycardia, and a serum leukocytosis. Confirmation of the diagnosis can be made only via joint aspiration. Other calcium deposition diseases such as hydroxyapatite (HA) may also present with an acutely inflamed joint.

Gouty Arthritis. Acute gouty arthritis is defined as the sudden onset of a painful joint owing to monosodium urate (MSU) crystal deposition, classically awakening the patient. The pain is so exquisite that even the bed sheets are painful. Any joint may be involved in acute gouty arthritis, and contrary to popular belief, the first metatarso-phalangeal (MTP) joint inflammation (podagra) is not always present. Nor is podagra always gout. The PEx reveals an acutely inflamed joint, but every joint should be inspected for possible involvement. Peripheral manifestations of hyperuricemia such as tophi on the ear and extensor surfaces may be visible. Gout is a result of either overproduction or underexcretion of uric acid. The former occurs most commonly in children and younger patients and the latter in middle-aged individuals with mild renal insufficiency. Precipitants of an acute gouty attack include factors that cause a shift in levels of serum urate such as alterations in fluid status, trauma, surgery, alcohol, acute illness, and medications. Medications frequently implicated include diuretics, contrast materials, and low-dose salicylates.

Evaluation of a patient with suspected acute gouty arthritis mandates joint aspiration. Fluid analysis reveals a leukocytosis often in the septic range. MSU crystals in white blood cells with compensated polarizing microscopy is diagnostic of acute gouty arthritis. An office microscope may be easily modified to allow such fluid inspection. The family physician is encouraged to learn such techniques. The sodium urate crystal is negatively birefringent and needle-shaped. The uric acid level at the time of the

acute attack is not helpful or predictive. A 24 urine uric acid is useful since a measurement greater than 1000 mg/dL indicates that the patient is an *overproducer of uric acid* (about 10% of cases) and a measurement below 800 mg/dL defines the *underexcretor*. This is important in tailoring management of chronic hyperuricemia. A serum creatinine is also necessary to evaluate renal function.

The management of the acute attack is directed at reduction of pain and inflammation. NSAIDs have become the first line of therapy in the treatment of acute gouty arthritis. They are most effective when used at the maximal anti-inflammatory dosages. Indomethacin is preferred, and ibuprofen, if prescribed, should be dosed at 3200 mg/day. Rapid tapering over the course of 4 to 7 days after the attack resolves is appropriate. Adverse effects of NSAIDs include renal toxicity, platelet dysfunction, gastrointestinal toxicity and bleeding, and drug interactions, including cross allergenicity with aspirin. Aspirin-induced asthma is also a contraindication for NSAID use.

Colchicine has a very narrow therapeutic toxic ratio. It may offer prompt relief, however, if given within the first few hours of the acute attack. Intravenous colchicine should not be used in patients with hepatic or renal disease and should be used in consultation with a specialist because of the potential life-threatening side effects. Oral colchicine may be administered as 0.5 to 0.65 mg tablets every 8 hours for the acute attack, tapering over the ensuing 5 days. When gouty attacks are frequent or serum-lowering urate therapy is being initiated, daily oral colchicine ranging from 0.5 mg to 0.6 mg 2 or 3 times daily reduces the frequency and severity. When NSAIDs and/or colchicine are contraindicated, corticosteroids are the treatment of choice. Intra-articular depot corticosteroids are often the best alternative in patients with multiple medical problems. Injection of the joint, however, should be deferred if there is a suspicion of a septic arthritis. Recent studies have demonstrated that a single intramuscular injection of 60 mg of TA is effective in acute gout. Long-term use of corticosteroids as anti-inflammatory agents is contraindicated.

It is recommended that acute attacks be treated as they arise, without much intercritical intervention. In those for whom the attacks become increasingly frequent (more than 2 to 3 per year) and severe, however, or if there is evidence of tophi or bony destruction, long-term therapy is needed. Patients with chronic tophaceous gout with underexcretion of uric acid may benefit

from uricosuric agents as well. All urate-lowering medications are initiated after the acute attack has resolved and the patient has been stable for a period of time. Uricosuric agents theoretically apply best to underexcretors of uric acid. Probenecid is the most commonly used uricosuric drug and is started at 0.5 g/day and gradually increased until the serum uric acid is 6 mg/dL or less. Patients must assure liberal fluid intake and have no history of nephrolithiasis or urine hyperacidity. Probenecid should not be used in patients with elevated serum creatinine. Sulfapyrazole (Anturane) is another uricosuric used less frequently because of potential bone marrow suppression and peptic ulceration.

Allopurinol (Zyloprim), a xanthine oxidase inhibitor, is ideally reserved for overproducers of uric acid, those with renal failure, or tophaceous disease. In reality, because of contraindications to uricosuric therapy and difficulty with compliance to assure adequate hydration, many underexcretors receive allopurinol to combat the uric acid load. This is not routinely recommended because of toxicity. Initial therapy of 50 to 100 mg/day of allopurinol is often sufficient for those patients with chronic gout. If warranted, the dosage may be gradually increased by 50 mg increments over weeks. Full dosage of 300 mg/day is often not necessary and increases risk of toxicity. The goal is to maintain the serum uric acid level to less than 6 mg/dL. Side effects of allopurinol include rash, gastrointestinal upset, fever, interstitial nephritis, granulomatous hepatitis, and toxic epidermal necrolysis. Serious vasculitis while rare, may be fatal. An allopurinol hypersensitivity syndrome may occur in 10% of patients with subsequent potential mortality.

Asymptomatic hyperuricemia is clearly a risk factor for the development of gout, though gout may never develop. The annual incidence of renal calculi is 1% in gout and 0.3% in asymptomatic hyperuricemics. Treating asymptomatic hyperuricemia has no value except for cases of overexcretion (>1000 mg/d), severe hyperuricemia of greater than 12 mg/dL, or in situations in which the acute urate load is secondary to tumor lysis. Urate-lowering therapy therefore is not justified in terms of risks and costs in asymptomatic hyperuricemia unless the patient is an overexcretor of uric acid, has a history of renal calculi, or has only one kidney.

Calcium Pyrophosphate Deposition Disease (CPPD). CPPD crystals are often responsible for an acute oligo-articular arthritis. However, they also present with a spectrum of disease manifestations. The rhomboid-shaped, positively birefringent crystal is less

strongly birefringent and therefore does not appear as “bright” as the MSU crystal. CPPD crystals are deposited in tendons, ligaments, articular capsule, cartilage, and synovium. The deposition appears to increase with advancing age, and pathologic evidence of CPPD, although clinically asymptomatic, may be present in more than half of individuals who are 80 years of age.

In pseudogout, one of the clinical manifestations of CPPD, the presentation is almost identical to that of acute gout, involving a similar joint distribution, precipitating factors (except medications), and degree of inflammation. Occasionally the attack of acute pseudogout may be somewhat less painful and often polyarticular at the onset. Joint aspiration is the only method with which to make the definitive diagnosis. Because the CPPD crystals are more difficult to detect, very careful examination of the fluid under compensated polarized microscopy is warranted. MSU crystals may be present concurrently.

OA is a secondary manifestation of CPPD, but the joint distribution is distinct. When “OA” is found in the less typical distribution of nonweight bearing joints, CPPD should be considered.

Symptomatic and asymptomatic CPPD may be discovered on routine radiographs. It is manifest by linear and punctate calcifications of the hyaline and fibrous cartilage that are less dense than bone.

Once CPPD is found either via joint aspiration or radiographs, it is imperative to screen for the underlying cause. CPPD may be hereditary or idiopathic (increasing with age), but many underlying metabolic abnormalities may be associated such as hyperparathyroidism, hemochromatosis, hypothyroidism, hemosiderosis, gout, hypomagnesemia, and familial hypocalcemic hypercalcemia. Screening for these diseases may be advisable.

Since no method is available to remove the offending crystal of CPPD, as is possible in gout, the treatment of CPPD is more difficult. NSAIDs and aspiration of the joints with or without corticosteroid injection may be helpful. Intercritical treatments are not recommended.

Hydroxyapatite (HA). HA represents other particles that deposit in soft tissues and joints that may excite an inflammatory response. HA deposition occurs commonly in periarticular structures such as shoulder tendons or poorly vascularized or previously traumatized tendons. Radiographic appearance of HA is a well-defined calcium deposit of a density similar to that of bone. HA is also the particle

responsible for the soft tissue calcifications seen in the various connective tissue diseases (CTD) that are discussed in Chapter 27.

Destructive arthropathies from HA have been termed “senile hemorrhagic arthritis” or “Milwaukee Shoulder.”

Trauma

Noninflammatory mono- or oligo-articular arthritis may also be secondary to trauma. Joint aspiration will yield a bloody effusion. The presence of fat or marrow fragments is indicative of a fracture. Depending on the duration of the swelling or the source of the trauma, the bloody synovial fluid should be sent for culture.

Polyarticular Inflammatory Arthropathies

Once an inflammatory process of three or more joints is established, further H&PE data will help sort through the differential diagnosis included under these polyarticular inflammatory arthropathies. Polyarticular inflammatory arthropathies often have accompanying constitutional symptoms, and although nonspecific, support systemic involvement.

Viral Arthropathies

The criteria for most autoimmune causes of an inflammatory polyarthritis include the duration of symptoms for at least, if not longer than 6 weeks. This is primarily to exclude the possibility of an infectious, specifically viral-induced, arthritis. The viral arthropathies, often mimicking the initial presentation of autoimmune arthropathies, disappear almost as quickly as they come, or at least within 4 to 6 weeks. They include rubella, parvovirus, Epstein Barr virus, cytomegalovirus, varicella, and mumps, rubella, and hepatitis A, B and C (3). Parvovirus B-19 or fifth disease (slapped cheek syndrome) can cause a severe, symmetric arthritis most commonly in adults, a red lacy rash on the trunk and extremities. The diagnosis is dependent on serum levels of IgM against parvovirus B-19 (5).

Rheumatic Fever

Rheumatic fever, although uncommon, has recently had some resurgence in the United States. This is an inflammatory condition following an infection with Group A beta-hemolytic streptococcus, affecting any organ of the body.

Rheumatic fever is rare in infants and individuals over age 30. The most common age range is 5 to 20 years. Most patients develop an acute migratory and occasionally additive polyarthritis. Symptoms are acute, occurring overnight, and associated with fever and myalgias. Any joint may be affected, but the large joints are more common. These symptoms are best treated with salicylates or NSAIDs and most episodes last 2 to 4 weeks. A chronic sequela of repeated attacks is Jacoud's arthropathy, seen in SLE, Ehlers-Danlos Syndrome and other CTDs.

Cardiac involvement is the most serious complication and may lead to valvular damage. Carditis, mitral regurgitation, mitral stenosis, and aortic regurgitation and stenosis may result. The likelihood of the above sequelae are greater with recurrences of rheumatic fever. Sydenham's chorea may occur long after the acute episode has subsided. Subcutaneous nodules on the extensor surfaces and erythema marginatum, which spares the face, are associated skin manifestations.

In evaluation of patients it is of importance to document the streptococcal infection. The serum antistreptolysin O titer (ASO) is most helpful. These titers may also be followed to note the progression and resolution of disease. Sensitivity is increased if ASO is combined with the antideoxyribonuclease B. The most important prognostic criterion is the presence of carditis.

After definitive confirmation of the diagnosis, treatment is with penicillin (erythromycin in the allergic patient). Bed rest is prescribed for those with cardiac manifestations, and the arthritis may be best treated with NSAIDs or high-dose salicylates (80 to 100 mg/kg/day, in divided doses) for a minimum of 3 to 4 weeks. Corticosteroids may shorten the course of the cardiac involvement but do not alter the amount of damage to the heart. Prophylaxis with benzathine penicillin is required monthly for those in endemic areas or on those with severe cardiac sequelae. The risk of a recurrent attack of rheumatic fever is higher in the 5 years after the initial attack. Prophylaxis therefore should continue for 5 years following the acute attack or until age 18.

Rheumatoid Arthritis (RA)

RA is a systemic autoimmune inflammatory disorder with many extra-articular features. This chronic arthropathy usually presents as a symmetric erosive arthropathy of the large and small joints. It most commonly spares the distal interphalangeal joints, and asso-

ated systemic features includes nodules, pleural and cardiac involvement, and vasculitis. The etiology of RA is unknown. It is possible that rheumatoid arthritis has no single primary cause (2), and the exact etiology of RA probably lies within a complex inter-relationship of infectious agents, genetics, and autoimmunity.

The clinical syndrome of RA involves features that vary among individual patients and within the same patient over time. The diagnosis is based on the clinical presentation of a symmetric inflammatory synovitis. This inflammatory synovitis may be demonstrated by a synovial fluid leukocytosis of greater than $2000/\text{mm}^3$ WBCs, a histologic demonstration of chronic synovitis, or radiographic evidence of erosions. Arthritis must be present for more than 6 weeks in order to exclude a transient arthropathy. Early in the disease, deformity and erosions may not be apparent, but a palpable effusion is detected. Aspiration is useful to exclude the presence of a crystalline arthropathy. The typical serologic features may not be evident, and during the initial evaluation other conditions must be excluded; the presentation may be insidious and in other cases more acute. The initial presentation of the rheumatoid arthritis often lacks the characteristic symmetry.

It is important to diagnose RA early in order to slow the irreversible structural damage that may result beginning within the first 2 years of disease. Although the actual inflammatory synovitis may follow a sine wave pattern of activity, the structural damage seems to progress.

Although RA may be diagnosed on H&PEx, some laboratory features aid in confirming the diagnosis and prognosticating. The rheumatoid factor (RF) is found in the serum of about 85% of the patients with RA, and a high titer correlates with severe unremitting disease, and with extra-articular manifestations. Once the diagnosis is established, repeating the test serves no purpose. Similarly, a positive RF in someone who has no clinical features of RA is of little value, as the test is not highly specific. Three percent of apparently healthy individuals may have positive RF, and this prevalence increases with age. RF is also frequently observed in other conditions such as SBE, chronic infections, malignancies, and other CTDs. Other nonspecific laboratory abnormalities in RA include hypergammaglobulinemia, anemia, thrombocytosis, and occasionally, hypocomplementemia. The erythrocyte sedimentation rate (ESR) varies according to the degree of inflammation in rheumatoid arthritis and has no prognostic or diagnostic

value. Clinical assessment of the patient is sufficient to reveal the degree of inflammation.

Up to 25% to 50% of patients with RA may have the characteristic subcutaneous rheumatoid nodules along tendon sheaths and in bursae during the active phases of disease. The nodules may also occur over pressure points and in organs such as the heart and eye and may disappear once the disease is under adequate control. Some patients may develop a vasculitis as part of the RA. The vasculopathies are commonly a dermal vasculitis and may be seen as small nail-fold infarcts or palpable purpura. The presence of such lesions located on the distal fingers or toes does not imply a systemic vasculitis. A meticulous examination for evidence of internal organ involvement, however, is indicated to rule out major vasculitis. The presence of ischemic ulcers represents the systemic vasculitis associated with RA.

Respiratory manifestations include inflammation of the cricoarytenoid joint. Patients may present with laryngeal pain, dysphonia, and difficulty swallowing. Stridor may occur and is a medical emergency. Rheumatoid lung disease may also take on various manifestations such as pulmonary nodules, interstitial fibrosis, pleural effusions, and bronchiolitis obliterans. The characteristic laboratory finding in the pleural fluid secondary to rheumatoid pleuritis is a distinctly low glucose level.

Inflammatory pericarditis and pericardial effusions may be seen in some patients with RA. This may progress to a constrictive pericarditis. Rheumatoid endocardial and myocardial nodules may become apparent clinically as valvular or embolic phenomena, conduction defects, and cardiomyopathy.

Gastrointestinal manifestations of RA are rare. Patients with associated Sjogren's syndrome, however, may have a dry mouth.

Neurologic symptoms include myelopathy related to the RA involvement of the cervical spine. RA in the thoracic and lumbar spine is rare. Tenosynovitis of the transverse ligaments of C1, which stabilizes the odontoid process of C2, may produce significant C1 and C2 instability. Careful neurologic examination should be performed, as well as flexion films of the cervical spine, if there is any question of a myelopathy or neck pain. Also, patients undergoing surgery should have preoperative flexion films. The greatest danger of C1 and C2 subluxation is with the extubation, when the patient may cough and the C-spine suddenly causes severe neurologic compromise including cord transec-

on. Signs of hyper-reflexia should alert the clinician to the presence of a myelopathy, since most patients with longstanding RA have hypoactive reflexes related to joint space contracture and muscle atrophy. Patients with RA also develop entrapment neuropathies. An abrupt onset of persistent peripheral neuropathy may signal mononeuritis multiplex caused by vasculitis. Selective nerve biopsy may confirm the diagnosis.

Felty's Syndrome (RA, splenomegaly and leukopenia) is most common with severe nodular disease. The leukopenia is selective involving mostly neutrophils, but the synovitis may be less active when the patient is neutropenic. Occasionally, thrombocytopenia may also be seen.

Traditionally, the treatment of RA has followed the pyramidal approach. At the base of the pyramid is education, rest, exercise, social services, rehabilitation therapy, and NSAIDs. The use of salicylates or NSAIDs is helpful in the alleviation of pain and inflammation. Those with early RA can be taught joint protection and adaptations for daily living.

Therapy of Rheumatoid Arthritis. When there is evidence of severe erosive and or inflammatory arthritis, an aggressive approach aimed at halting disease progression is definitely in order. While some of the existing therapies are considered to be disease modifying, this modification of the natural course is difficult to prove in scientific studies. The slow-acting antirheumatic drugs (SAARDs) are used in hopes that joint destruction will be reduced or slowed. These second-line agents are sometimes referred to as disease modifying antirheumatic drugs. They have significant toxicity, which requires close monitoring. While no consensus exists as to which SAARDs should be used and in what order, most rheumatologists will agree the treatment must be individualized, and the initial use of less toxic therapy is preferred. It is appropriate for the primary-care physician to obtain a rheumatology consultation to select appropriate therapy with these drugs. One of the "safer" disease modifying antirheumatic drugs is hydroxychloroquine (Plaquenil). It may be given as 200 mg by mouth twice a day, and its effect will be seen in 8 to 12 weeks. Baseline ophthalmologic slit lamp, fundoscopic, and Anslar grid examination with interval examinations every 6 months can detect early retinal changes and minimize the chance of permanent visual impairment. Methotrexate, a folic acid antagonist, is now first-line treatment. It can be given orally or by injection with

the usual starting dosage of 7.5 mg/wk. Response is seen within 1 1/2 to 2 months. If tolerated, dosages can be increased to 15 to 20 mg per week. Because of liver toxicity, alcohol consumption, gross obesity, and diabetes are contraindications to methotrexate use. Concomitant therapy with sulfonamide containing compounds and the presence of HIV infection are also contraindications. Close monitoring includes monthly complete blood cell counts and liver enzyme studies every 2 to 3 months. Persistent elevations of transaminase enzymes or significant hypoalbuminemia may indicate the need for liver biopsy. The latter is not indicated for most patients on methotrexate therapy.

Gold salts have been used in the treatment of RA for more than 60 years. Its status as the standard with which other treatment programs are compared has been taken over by methotrexate. Gold salts are given by deep intramuscular injection initially weekly and eventually extended to a monthly basis. These patients must be monitored with a urinalysis and blood and platelet counts before each injection.

Other therapies that are more toxic but that are used to treat RA include azathioprine, sulfasalazine, penicillamine, cyclophosphamide, and cyclosporin. These fall under the third tier of therapy along with experimental drugs. Only azathioprine and penicillamine are approved at this time. Rheumatologic consultation may be of value when deciding third-tier therapy.

The pyramidal approach to therapy has been modified and replaced by a reverse approach with the initiation of aggressive treatment and/or multiple medications. This treatment plan is similar to the approach oncologists use in malignancy.

Corticosteroids play a very limited role but are useful in the treatment of vasculitis associated with RA. The glucocorticoids have both anti-inflammatory and immunosuppressive effects but have not been shown to be disease modifying.

Juvenile Chronic Arthritis (JCA)

Although many similarities exist between the adult and pediatric autoimmune diseases, important differences also exist. These diseases will affect the growth and development of the child, and parental involvement and care will affect the compliance, prognosis, and eventual outcome. The nomenclature regarding the pediatric arthropathies has been evolving, and recently the term JCA has been added as an inclusive term encompassing juvenile

rheumatoid arthritis (JRA) and its three subtypes, along with juvenile ankylosing spondylitis (JAS).

Juvenile Rheumatoid Arthritis (JRA). JRA encompasses three variants: systemic onset (Still's disease), polyarticular onset, and pauciarticular onset. Approximately 10% of JRA is of systemic onset. The sex distribution is equal, and it can begin at any age. Clinical manifestations include spiking fevers with an evanescent salmon rash, diffuse lymphadenopathy, hepatosplenomegaly, pericardial and/or pleural effusions. The children are quite ill, and muscle atrophy and weight loss may be severe. The ANA and RF are usually negative, but there may be a leukocytosis and anemia.

The episodes of systemic onset JRA are usually self-limited, but close attention must be paid to cardiac, pulmonary, and hematologic involvement. Many of these children will develop a chronic polyarthritis often years later, and some will suffer severe, chronic arthritis that continues with or without continued systemic manifestations.

Polyarticular JRA is defined as involvement of 5 or more joints. Girls are affected more frequently than boys, and fatigue, malaise, weight loss, low-grade fever, mild organomegaly, adenopathy, anemia, and growth retardation are frequent. The joints are often symmetrically involved, and there is cervical spine involvement, as well. Children may be RF positive and ANA positive. Those with positive RF tend to have more erosive disease, with rheumatoid nodules and vasculitis. The polyarticular variant tends to resemble the adult RA and has a worse prognosis. Growth disturbances are well recognized in systemic and polyarticular JRA. Micrognathia due to temporomandibular arthritis is common.

Those children with fewer than 4 joints affected within the first 6 months of disease are termed pauciarticular. This subtype affects girls under the age of 6, is negative for RF, and in some instances has a positive ANA. Systemic features do not occur, and the prognosis for joint function is good. Many of the children with this type of JRA develop inflammation of the anterior uveal tract, which may lead to grave consequences including blindness. Since patients are frequently asymptomatic, early detection and treatment requires *all* pauciarticular JRA patients to have initial and periodic ophthalmologic slit lamp examinations. JRA is the leading cause of blindness in children in the United States. A positive ANA is a marker for this and should lead to even more vigilance.

Another group of pauciarticular JRA patients are predominantly boys ages 8 to 10. These patients are RF and ANA negative but have a high frequency of HLA-B27 markers. These boys have inflammation at tendinous insertions, sacroiliitis, and iridocyclitis. The family history may be positive for spondyloarthropathies or associated conditions.

Treatment of the JCA requires extensive patient and parent education. The treatment goals are to reduce pain and inflammation, allow for as much normal growth and development as possible, and restore and maintain function. Aspirin, although the most effective and the least expensive anti-inflammatory agent, is difficult to take because of frequent dosing and risky because of the associated Reye's syndrome. NSAIDs have become the treatment of choice except in Still's disease, for which salicylates are best. Intramuscular gold therapy and oral weekly methotrexate are usually initiated by rheumatologists if the foregoing approaches fail.

Spondyloarthropathies (SPA)

The SPA affect the spine as well as peripheral joints. The term *seronegative spondyloarthropathies* is confusing and should be avoided. The presentation is that of an asymmetric peripheral arthritis along with low back stiffness. Involvement of the distal interphalangeal (DIP) joints is common. Asymmetry, DIP, and spine involvement distinguish the SPA from classical RA. There is usually no need, therefore, to test for RF in such a patient. SPA is often associated with extra-articular manifestations. The history should include or exclude the possibility of chronic gastrointestinal or genitourinary inflammation, ocular inflammation, psoriaform skin and nail lesions, and lesions involving the heart valves, and lungs. The diseases include ankylosing spondylitis (AS), reactive arthritis, Reiter's syndrome, psoriasis, and inflammatory bowel disease (IBD)-associated arthritis. There is a striking association of most of these disorders with HLA-B27. Some patients, however, are HLA-B27 negative, and many patients who are HLA-B27 positive do not develop SPA. The test is used primarily for epidemiologic studies.

The hallmark of the SPA is a sacroiliitis, either symmetric or asymmetric. Radiographic evidence of sacroiliitis is manifested by sclerosis as well as erosive changes along the sacroiliac joint. Syndesmophytes forming a bamboo spine is also classic.

The peripheral arthritis in many of the SPA reveals central cartilaginous erosion, rather than the marginal erosions seen in RA.

Ankylosing Spondylitis (AS). AS primarily affects the axial skeletal joints. For the most part, it is a disease of young males under the age of 40. The onset of the arthropathy is usually quite gradual, and the sacroiliitis is very symmetric, progressing to fusion. Approximately 25% of patients will have peripheral joint involvement and/or eye involvement. There is a rare associated lesion of aortic or mitral insufficiency.

The diagnosis is based on clinical features and x-rays. Most commonly, the patients complain of back pain and stiffness, which is worst in the morning and improves with physical activity or heat.

Although the physical signs may be minimal early in the disease, close attention to the lumbar spine is necessary. Direct measurement of spinal flexion, using the Schober test, should be done if AS is suspected. A 10 cm distance from a point at the intergluteal fold (sacroccocygeal junction) is marked off cephalad. With forward bending, the two points should move apart to a distance of 15 cm. Chest expansion should be measured also at the nipple line at deep inspiration and expiration.

The most common extraskeletal involvement is “acute” anterior uveitis, which occurs in 25% to 30% of patients at some time in the course of their disease (6), typically unilateral. Neurologic symptoms usually occur after the spine has fused, sometimes leading to fracture, pseudoarthrosis, severe pain, paraplegia, or even quadriplegia. Urinary and fecal incontinence, sensory loss in the sacral distribution, impotence, and occasionally loss of ankle reflex are manifestations of a cauda equina syndrome (6).

Reiter's and Reactive Arthritis. Although the exact trigger for the spondyloarthropathies is unknown, many infectious agents give rise to syndromes. The most common is that of Reiter's syndrome, which encompasses the triad of nongonococcal urethritis, uveitis, or conjunctivitis and arthritis. This is covered in Chapter 16.

Psoriatic Arthritis. Approximately 7% to 15% of patients with psoriasis develop an associated arthropathy. The psoriasis may be present many years before the arthritis develops, it may begin at the same time as the arthritis, or it may present after the arthritis has already been established. It is often the patient in whom the

exact diagnosis of the arthritis remains elusive who then comes in one day with a psoriatic patch and the diagnosis is then made.

Psoriatic arthritis has 5 main patterns: distal interphalangeal pauciarticular involvement with nail disease; asymmetric polyarthritis with enthesopathies and sausage digits; spondylitis; a severe destructive arthritis mutilans, and RA-like disease. The nail changes associated with psoriasis include nail pitting and onycholysis (lifting of the nail).

Management of psoriatic arthritis is like that of rheumatoid arthritis. Dermatologic consultation is often required but may not impact the course of the axial arthritis. The peripheral arthritis may respond with improvement of the skin. For those individuals with progressive polyarticular arthritis, methotrexate is the first line of therapy for both the arthritis and skin manifestations. Injectable gold is also an option. Antimalarials need to be used with caution since they may cause a flare of the skin disease.

IBD. Crohn's disease and ulcerative colitis are associated with both a peripheral and axial arthritis, which is included in the SPA group. The peripheral arthritis of IBD is pauciarticular involving the large and small joints of the upper or lower extremities. It is asymmetric and nondestructive. There may be an associated enthesopathy. The axial involvement is like AS. The activity of the peripheral arthritis tends to parallel the activity of the IBD. The axial arthropathy proceeds independently from the activity of the IBD. Bowel resection or surgery does not alter the course of the axial arthritis.

Treatment is similar to that of other SPA but caution must be employed regarding exacerbation of ulcerative colitis with NSAID use. Sulfasalazine, useful in the treatment of IBD, alleviates the peripheral arthritis. Although local intra-articular corticosteroid injections may be occasionally useful, systemic corticosteroids are not indicated as treatment of the arthritis unless for primary control of the underlying IBD.

NERVE ENTRAPMENT SYNDROMES

Carpal tunnel syndrome (CTS) is an entrapment syndrome involving the median nerve. In addition to neuropathic symptoms, patients often complain of diffuse hand swelling or an achy, "arthritic" feeling of the hands. Classically patients with CTS complain of the hand(s) falling asleep and numbness and tingling in-

involving the thumb, plus the radial three and one-half digits. This often awakens patients at night, and they must shake the hands to “wake them up.” These sensations also occur whenever the hand is held in a flexed position, increasing the pressure on the median nerve, as in driving or holding reading material. The pain may appear as a writers cramp, radiate proximally to the elbow, or result in cold sensitivity of the fingers. The PEx may reveal positive Tinel’s and /or Phalen’s sign. In severe cases, motor strength of the thumb and thenar atrophy may be decreased. Electromyography and nerve conduction study are useful in quantifying the conduction of the median nerve. This test is not 100% sensitive, and therefore the diagnosis is still primarily clinical.

The most important portion of the work-up of CTS is defining the etiology. Although known as an “overuse” syndrome, it often may herald a more severe underlying systemic disease. Patients should be screened for endocrinopathies such as diabetes, hypothyroidism, and acromegaly which may be subclinical. CTD such as systemic lupus erythematosus, rheumatoid arthritis, and amyloidosis may initially present with CTS. Malignancies and multiple myeloma need to be considered as well. CTS may also be related to the third trimester of pregnancy and the postpartum period.

Early recognition and treatment of CTS is essential to prevent irreversible muscle weakness. Treatment of any underlying illness is important. Conservative therapy consists of splinting of the involved wrist with a functional cock-up wrist splint that maintains the wrist in neutral to 10 degrees of extension. These splints should be worn while sleeping and also during daytime hours when performing activities that increase pressure on the median nerve. NSAIDs are occasionally helpful in relieving the associated pain and inflammation. If the symptoms persist, corticosteroid injection may be attempted cautiously. Surgical release is indicated if conservative measures fail or there is evidence of motor weakness.

Tarsal tunnel syndrome (TTS) is a condition similar to but much less prevalent than CTS that affects the posterior tibial nerve when compressed by the flexor retinaculum located posteriorly and inferiorly to the medial malleolus. Patients report numbness and tingling often with an associated burning sensation of the toes and soles that extends proximally to the medial malleolus. A Tinel’s sign may be elicited by tapping over the

flexor retinaculum. The same systemic diseases that cause CTS may cause the TTS. TTS may also arise secondary to trauma, dislocation, hypermobility, and occupational factors. Shoe corrections and corticosteroid injections may provide relief, but often surgical decompression is necessary.

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Musculoskeletal Problems in Children

Russell Wenacur and James B. Tucker

INTRODUCTION

Complaints of musculoskeletal pains during childhood or adolescence are not uncommon. The majority of these complaints are benign and self-limited. The practitioner, however, must have a high index of suspicion for less common, more serious causes of illness to avoid significant morbidity and mortality in affected children.

Musculoskeletal disorders in children cover a wide range of illnesses, which can be congenital or acquired. Lower extremity problems are not uncommon and may manifest themselves as a limp or as obvious deformity. A child's complaint of pain and/or limping may be a significant source of anxiety for parents. It is the role of the clinician to assess the situation, make a diagnosis and give reassurance to the anxious parents. A detailed history, including trauma, duration of symptoms, inciting events, and complete physical examination along with appropriate laboratory and radiographic analysis remain the mainstay of diagnosis and treatment.

GAIT AND POSTURE ISSUES IN FIRST YEAR OF LIFE (AND BEYOND)

Developmental Dislocation of the Hips

Abnormalities in posture or gait frequently prompt a physician's evaluation. Pain, duration of symptoms, or location may be

helpful clues to the diagnosis, but are often difficult to elicit from small children. The etiology of developmental dislocation of the hips (DDH) is felt to be multifactorial, with mechanical factors (positional deformities within uterine cavity) in addition to ligamentous laxity playing a role in its development. Females are affected 6 times more often than males, and the incidence is approximately 1.5 per 1000 live births. Approximately 20% of cases have a positive family history of DDH (1, 2). The left hip is involved in 60% of cases, the right hip in 20%, and 20% are bilateral (2).

DDH has three degrees of severity (in ascending order): subluxatable, dislocatable, and dislocated hips. The Barlow (dislocation) and Ortolani (reduction) maneuvers are the standard for clinical diagnosis of DDH. In cases where physical examination is equivocal or abnormal, ultrasound is the radiologic technique of choice (3). Prior to 6 months of age, when the femoral head and acetabulum are mainly cartilaginous structures, sonography can identify and/or quantify degrees of hip instability without ionizing radiation (3). Universal sonograph screening of newborns is not recommended, unless there is a positive family history, but careful examination of the hips in the newborn nursery and at subsequent well-child exams in the first 6 months of life is critical.

In milder forms of instability like subluxation (partially dislocatable hip), observation and reexamination at 1 month of life is the usual recommendation (4). This may represent "physiologic laxity" and spontaneously improve with time. Dislocatable and dislocated hips are generally treated at the time of diagnosis by harness apparatus under the supervision of pediatric orthopedists.

Complications of untreated DDH include avascular necrosis of the femoral head (Perthe's disease), persistent dysplasia with future gait abnormalities, and persistent dislocation of the hip leading to osteoarthritis. Early detection is the key to limiting morbidity later in life.

Intoeing

Intoeing is a relatively common phenomenon found in infants and children. Metatarsus adductus (MA), internal tibial torsion (ITT), or excessive femoral anteversion (EFA) are the most common causes of intoeing (5).

MA is noted as a "C-shaped" curve in the lateral border of the foot, rather than a straight border. It presents in approximately 1:1000 live births and has been associated with DDH (5). It is gen-

erally felt to be a result of intrauterine molding. Approximately 85% to 90% of cases spontaneously resolve by 1 year of age, and approximately 95% resolve during childhood. Treatment initially involves stretching exercises to increase flexibility and correct the deformity. If stretching is inadequate to correct the deformity by 8 months of age, rigid casting may be appropriate (even though many cases will spontaneously resolve by 1 year of age). Even untreated cases rarely contribute to significant morbidity (5, 6).

Internal tibial torsion (ITT) usually presents to the physician at walking age, although it is routinely found in the newborn (secondary to intrauterine position). Clinically, it is identified by observing the child whose kneecaps point straight, but whose toes point inward during ambulation. In addition, the medial malleolus is located posteriorly in relation to the lateral malleolus. Like metatarsus adductus, about 95% of cases resolve spontaneously by 8 years of age. Nonsurgical treatments have shown no benefit. Studies of surgical intervention have shown high complication rates. Although complete resolution of ITT is the rule, it cannot be guaranteed. Long-term sequelae of untreated ITT are rare, however, and parents must be counseled and reassured prior to final decision making (5, 6).

Excessive femoral anteversion (EFA) is the most common cause of intoeing and usually presents in early childhood. Clinically, when standing, the kneecaps are noted to be pointing inward along with intoeing. Clinical measurements of hip rotation show increased internal over external rotation of the hips. Although hip angle measurements change between infancy and adulthood, persistent EFA has been loosely associated with osteoarthritis and gait disorders. Bracing or casting has shown no benefit, and surgical osteotomy is the only acceptable treatment. Complication rates are high, making this a treatment only for severe or persistent cases (5). Again, a majority of these cases resolve spontaneously, and close observation and parent education are mandatory.

MOST COMMON CAUSES OF ARTHRALGIA IN CHILDREN

Limping and joint discomfort are the most common sign and symptom of arthralgia in children. The limping child presents a significant challenge to the diagnostic skills of the physician. Careful history and physical examination can aid in ruling out trauma

or infection as potential causes for arthralgia. Causes of limping may be categorized by the age of the child. In infants and toddlers, angular deformities, DDH, or developmental delay (e.g., cerebral palsy) must be considered. In children, toxic synovitis, Legg-Calve-Perthes disease, postinfectious arthritis, and juvenile rheumatoid arthritis (JRA) must be considered. In adolescents, slipped capital femoral epiphysis (SCFE), Osgood-Schlatter's disease, postinfectious arthritis, scoliosis, and JRA must be considered. In all ages septic arthritis, osteomyelitis, and tumor must be considered and swiftly ruled out.

DDH and angular deformities in infants have been discussed. Toxic synovitis is a commonly occurring cause of limp in children under 10 years of age. It is recognized as a self-limited illness with joint pain (most commonly hip pain), inflammation, and effusion. It is more common in males (approximately 4:1) and is generally unilateral. Clinically, limitation of hip motion (medial rotation and abduction) with pain and, rarely, mild joint swelling are noted. The patient may have a low-grade fever, but laboratory studies (WBC, ESR) are usually normal or slightly elevated (1, 2, 7). This condition is usually benign and self-limited with spontaneous resolution in greater than 70% by 1 week. However, significant overlap in symptoms occurs with the more serious septic arthritis, and care must be made to make the correct diagnosis. Treatment includes activity as tolerated and non-steroidal anti-inflammatory medication with slow return to full activities after resolution of pain.

Septic arthritis is a medical emergency, and prompt diagnosis and treatment are critical. Infectious arthritis accounts for approximately 5% to 10% of all childhood arthritides and is monoarticular in 90% of cases (1, 2, 7-9). In contrast to toxic synovitis, a child with septic arthritis usually appears ill. The child likely will have a fever, joint pain, swelling, and extreme tenderness. The WBC and ESR are increased. Radiographs can help rule out osteomyelitis or Legg-Calve-Perthes disease. Joint fluid aspiration is considered the definitive test for diagnosis. Joint fluid should be sent for *culture and stat Gram stain*, cell count, and glucose. Gram stain may be revealing in 30% to 50% of cases, but culture results are the gold standard for directing therapy (9, 10). Cell count may show predominance of neutrophils, similar to that of the CBC. If the patient fails to respond to antibiotics, or the diagnosis remains in question, arthroscopic

evaluation may be warranted. Infecting organisms differ according to patient age as well as route of infection.

Gram-positive cocci (especially *S. aureus* and pyogenic streptococci) are by far the most common infecting organisms. But, the practitioners must consider group B streptococci in neonates and *Hemophilus influenzae* (Gram-negative rod) in younger children with septic arthritis. It is important to institute broad spectrum intravenous antibiotic coverage until culture results are available, since reports of pseudomonas and *K. pneumoniae* infection have also appeared in the literature (9).

Legg-Calve-Perthes disease (avascular necrosis of the femoral head) is characterized by interruption of blood flow to the developing femoral epiphysis, with resorption and replacement by immature bone. The etiology is unknown. It is more common in males (approximately 5:1) and is usually seen in children between 4 and 8 years of age. The child initially notes a pain-free limp after activities. Subsequently the child develops hip, thigh, and knee pain (11). Progressive muscle spasm limits abduction and internal rotation. X-rays reveal a "moth-eaten"-appearing femoral epiphysis with irregular contours. Prompt orthopedic referral is necessary. Treatment includes maintaining range of motion of the joint with containment of the femoral head in the acetabulum. Bracing or surgery may be necessary (12). Prognosis is generally good in cases of early diagnosis and treatment.

In adolescence slipped capital femoral epiphysis (SCFE) is the most common cause of hip pain (1, 2, 11, 12). It is more common in males (approximately 2 to 5:1) and has an incidence of approximately 1:100,000 to 4:100,000. It is characterized by displacement of the femoral head from the femoral neck secondary to shearing forces applied to the area prior to growth plate closure. It is most common during the pubertal growth spurt, and is associated with other disorders including obesity, hypothyroidism, and growth hormone deficiency.

SCFE presents similarly to Legg-Calve-Perthes disease. The initial pain is usually worse in SCFE, and the patient holds the limp in lateral rotation with limitation of flexion, and internal rotation. The patient walks with a limp, and limb shortening may be evident. SCFE is an orthopedic emergency, and prompt referral to an orthopedist is mandatory. Nonweight bearing to prevent further slippage and possible operative fixation may be indicated (11, 12).

Osgood-Schlatter's disease usually affects athletic males during the pubertal growth spurt. It is characterized by a "traction apophysitis" of the tibial tubercle from microtrauma. Localized tenderness and swelling over the tibial tubercle is noted, but there is no joint effusion. The pain is worsened with activity and direct pressure to the tubercle and improved with rest. Treatment depends on intensity of pain. Activities are permitted as tolerated and nonsteroidal anti-inflammatories are used if needed. The condition usually remits after fusion of the tibial tubercle with the diaphysis (1). This usually occurs between ages 9 and 15, but may persist until the end of the pubertal growth phase.

Postinfectious arthritis and JRA are discussed in Chapter 25.

Bone tumors, brain tumors, and spinal cord tumors may rarely present with a "limp." Discussion of these conditions is beyond the scope of this chapter, but a high index of suspicion is necessary to rule out these potentially lethal diseases.

Rheumatic fever is covered in Chapter 25.

INFLAMMATORY ARTHRITIDES IN CHILDREN

Inflammatory arthritides in children encompass a broad category of illnesses. The differential diagnosis poses a particular challenge for the primary-care physician. Compounding this broad differential is the fact that most inflammatory arthritides are relatively benign, self-limiting, and of low potential for morbidity or mortality, whereas others are emergencies and require prompt diagnosis and treatment to prevent long-term morbidity and mortality. It is not always easy to distinguish between the entities, but history, clinical examination, and a high index of suspicion can help reach the appropriate diagnosis.

The term *inflammatory arthritis* refers to a condition manifest as pain, swelling, tenderness, erythema, and/or decreased range of motion in a joint secondary to the body's inflammatory response. This response may be as a result of trauma, or a response to infection (septic arthritis, toxic synovitis, osteomyelitis, lyme arthritis) or as a result of immune-mediated responses (reactive arthritis secondary to streptococcal infection, salmonella or shigella enteritis, yersinia enteritis chlamydia urethritis, many types of viral infections [Parvovirus B19, HIV] or juvenile rheumatoid arthritis). Crystal-induced arthritis is much less common in children than adults, and will not be covered here.

Traumatic arthritis is usually suggested by history. Conservative therapy with rest, ice, and nonsteroidal anti-inflammatories are usually sufficient treatment unless fracture or joint deformation is noted on x-ray. Less obvious forms of trauma include microtrauma events (Osgood-Schlatter's disease, Patella-femoral syndrome). Conservative therapy including physical therapy is again indicated, with referral to an orthopedist for patients who fail to respond.

Infectious arthritides such as septic arthritis and toxic synovitis have already been discussed. Osteomyelitis is a serious medical condition that requires prompt hospitalization and initiation of appropriate antibiotic therapy. Delay in diagnosis or treatment can result in additional morbidity and/or mortality.

Many other bacterial and viral illnesses can result in postinfectious arthritis. For example, patients with arthritis following streptococcal infection but who do not meet Jones' criteria for rheumatic fever are considered to have poststreptococcal reactive arthritis (13). Enteric infections with salmonella, shigella, campylobacter, and yersinia enterocolitica have all been associated with postinfectious "reactive" arthritis (13, 14). Particularly important is the association with chlamydia urethritis and reactive arthritis. Sexually active adolescents with multiple partners who fail to take precautions against sexually transmitted diseases are at a particularly high risk.

Viral illnesses may cause a postinfectious arthritis as well. Parvovirus B19 (fifth disease) frequently results in a postinfectious arthritis (13, 14). Measles, mumps and rubella vaccination has been implicated in temporary gait disturbances and postimmunization arthritis (10, 11, 15). Natural infection with the above viruses has also been associated with arthritis.

The exact mechanism for the arthritis following these infections is unknown. It is felt to be secondary to an accelerated immune response and to cell activation. Although direct infection of the joints is uncommon in these illnesses, bacterial and viral DNA has been found in joint fluid analysis, and this may be acting as an antigenic stimulus for T-Cell activation (13, 14).

HIV infection has been associated with reactive arthritis. Except for HIV, the arthritis associated with the infections listed above is generally benign and self-limiting. They rarely result in permanent arthritis or joint deformities, and generally resolve in a short period of time.

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Approach to the Connective Tissue Diseases

Lori B. Siegel and Eric P. Gall

APPROACH TO THE CONNECTIVE TISSUE DISEASES (CTD)

Criteria for most of the CTDs have been established (1). These criteria are most useful in research settings but also act as guides to categorizing signs and symptoms of CTD. They are not, however, diagnostic criteria. Gray zones in diagnosis frequently exist. Specific laboratory tests of the immune system may be helpful but again they alone do not make a diagnosis. Laboratory testing should be reserved for lending support to an already suspected clinical diagnosis. One does not make a diagnosis based on a laboratory test. Positive RF and ANA are seen in a variety of non-rheumatologic conditions and even in otherwise normal people.

RAYNAUD'S PHENOMENON (RP)

RP is manifest by the classic blanching, cyanosis, and erythema of the digits upon exposure to cold or emotional stress, and the true diagnosis is reserved for those with the characteristic tricolor change. The toes, tip of the nose, and penis may also be involved. The etiology is that of vasospasm along with a structural abnormality of the blood vessel resulting in infarction of the digital fat pad secondary to prolonged episodes of vasospasm. Secondary RP, which may accompany any connective tissue disease, is not diagnostic of a specific entity. A majority of patients with the above vasospastic changes have primary RP or Raynaud's disease. These

patients have no underlying connective tissue disorder. When patients present with primary RP a thorough history and physical examination (H&PEx) is sufficient in searching for evidence of a related CTD.

Laboratory screens for CTD without historical or physical support are not worthwhile. RP may antedate CTD by many years. On the other hand some patients may have a positive ANA and never develop systemic lupus erythematosus.

Treatments for RP, primary or secondary, are similar and consists of practical measures such as wearing gloves and keeping the body warm in cold weather, air conditioning or while shopping in the refrigerated sections. Some gloves can be warmed electronically. Because of an alteration in blood flow close attention to trauma and avoidance of infection is necessary. Medical management in some cases may include the use of calcium channel blockers such as long-acting nifedipine, alpha adrenergic antagonists, serotonin receptor blockers, or topical nitroglycerine.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

SLE is referred to as the prototype of autoimmune disease. It is actually a constellation of signs and symptoms. It is a disease that affects women 9 times more frequently than men in the ages 15 to 54, and is more common and more severe in those of Hispanic, African and Asian descent. In the general population, the chance of getting SLE is 0.05%; in first-degree relatives of someone with SLE that risk increases to 0.4% to 5%. Monozygotic twins have a 50% concordance rate.

The inclusion of SLE in a population study rests on meeting 4 of 11 criteria established for SLE (Table 27.1). These criteria demonstrate the amount and extent of abnormalities that occur clinically with SLE. When these abnormalities occur in a setting of multisystem disease and autoantibodies, the clinical diagnosis is suggested. Rheumatologic consultation may help secure the appropriate diagnosis. Constitutional symptoms of fatigue and malaise are common. Fever is present in 5% of cases. Alopecia is described as significant patches of hair loss on the pillow or while washing. A classic malar rash, spanning the bridge of the nose and sparing the nasolabial folds, may be quite subtle. The rash is commonly photosensitive; exacerbations occur even secondary to sunlight through a car windshield. Patients with SLE often have a nondeforming, nonerosive arthropathy with reducible

Table 27.1.
1982 Revised criteria for the classification of systemic lupus erythematosus.

Criterion	Definition
1. Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
2. Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
3. Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
4. Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
5. Arthritis	Nonerosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling, or effusion
6. Serosistis	(a) Pleuritis-convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion or (b) Pericarditis-documented by ECG or rub or evidence of pericardial effusion
7. Renal disorder	(a) Persistent proteinuria greater than 0.5 grams per day or greater than 3+ if quantitation not performed or (b) Cellular casts-may be red cell, hemoglobin, granular, tubular, or mixed
8. Neurologic disorder	(a) Seizures in the absence of offending drugs known metabolic derangements; e.g., uremia, ketoacidosis, or electrolyte imbalance or (b) Psychosis in the absence of offending drugs or known metabolic derangements, e.g., uremia, ketoacidosis, or electrolyte imbalance
9. Hematologic disorder	(a) Hemolytic anemia with reticulocytosis or (b) Leukopenia, less than $4,000/\text{mm}^3$ total on two or more occasions or (c) Lymphopenia, less than $1,500/\text{mm}^3$ on two or more occasions or (d) Thrombocytopenia, less than $100,000/\text{mm}^3$ in the absence of offending drugs

Table 27.1 (continued).
1982 Revised criteria for the classification of systemic lupus erythematosus.

Criterion	Definition
10. Immunologic disorder	<div> <div>(a) Positive LE cell preparation</div> <div>or (b) Anti-DNA: antibody to native DNA in abnormal titer</div> <div>or (c) Anti-Sm: presence of antibody to Sm nuclear antigen</div> <div>or (d) False-positive serologic test for syphilis known to be positive for at least 6 months and confirmed by <i>Treponema pallidum</i> immobilization or fluorescent treponemal antibody absorption test</div> </div>
11. Antinuclear antibody	<div>An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs known to be associated with "drug-induced lupus" syndrome</div>

The purpose classification is based on 11 criteria. For the purpose of identifying patients in clinical studies, a person shall be said to have systemic lupus erythematosus if any four or more of the 11 criteria are present, serially or simultaneously, during any interval of observation.
 Reprinted with permission from: Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus (SLE). *Arthritis Rheum* 1982;25:1271-1277.

subluxations and ulnar deviation. There is also an increased risk of avascular necrosis (AVN), independent of steroid use. Persistent joint pain especially in the hip or knee should prompt an investigation for AVN, even with normal plain radiographs. Mucocutaneous lesions may be asymptomatic and must be searched for on physical examination. The vascular manifestations range from livido reticularis, a reddish cyanotic reticular pattern, to RP in 20%, as well as digital ulceration and full blown vasculitis in 10% to 20%. The most dire and serious complications are those involving the kidneys and CNS.

Routine laboratory investigation will reveal further evidence of SLE. The CBC offers a bounty of information. An anemia, if present, may be that of chronic disease or the autoimmune hemolytic anemia. The white cell count may reveal characteristic leukopenia, and specifically lymphopenia. Evidence of immune thrombocytopenia is not uncommon. The chemistry for renal function is not as valuable since patients with active yet early lupus nephritis may have a normal creatinine. The most valuable tool in assessment of renal involvement is the urinalysis with attention to the sediment. Evidence of red blood cells, protein and red blood cell casts indicates active renal involvement. A 24-hour urine collection will also aid in quantification of protein loss and creatinine clearance.

Specialized tests including antinuclear antibodies (ANA) and extractable nuclear antigens (ENA) are useful in supporting a suspected diagnosis but in general are not useful prognosticators. There are many false positive results secondary to infections, malignancy, medications, and various medical conditions. Four major patterns of the ANA are clinically useful. The homogeneous pattern is the most common. Although seen in SLE, it may be detected in a variety of connective tissue diseases and it is always seen in drug-induced lupus. It is the most frequent pattern of the "false positive" ANA secondary to malignancy and infection. The rim or peripheral pattern is practically unique to SLE and signifies antibodies to double stranded DNA (anti-dsDNA). It correlates with renal and/or central nervous system involvement. While not all patients develop renal or CNS disease, if positive, they should be monitored diligently. The speckled pattern is seen in SLE and overlap (mixed connective tissue disease), and portends a better prognosis than the rim pattern. It may also be seen in RA and systemic sclerosis, both limited and progressive.

The nucleolar pattern of immunofluorescence is rare in SLE but seen most commonly with RP, Sjogren's syndrome and systemic sclerosis. Common ENAs include the anti-Smith (anti-Sm), which is the most specific for SLE, and soluble ribonucleo-protein (s-RNP), which is a nonspecific marker for mixed connective tissue diseases.

Cytoplasmic antibodies include Anti-Ro (SSA) and Anti-La (SSB) originally described and seen in Sjogren's syndrome. SSA in a pregnant woman may be associated with neonatal lupus and congenital heart block since it crosses the placenta and interferes with formation of the cardiac conduction system. It should be performed in pregnant lupus patients. It is also usually positive in "ANA negative lupus."

Most patients evolve over time and may not present with clinically evident SLE at the first evaluation. Treatment of SLE is primarily symptom-based, and the presenting symptoms should be treated. The patient needs education and support once the diagnosis is considered or made. Mortality curves and survival have changed dramatically, and because of increased suspicion and sensitive laboratory tests, many milder cases of SLE with a good prognosis are diagnosed. The majority of the lay public, however, still equate SLE with severe disease, renal failure, and death. A discussion of possible SLE without the proper education and support may lead to severe fear and psychologic effects. The goal in the treatment of SLE is to strike a balance between suppression of disease and minimizing drug toxicity.

Patients with arthritis should be treated with anti-inflammatory doses of NSAIDs. The skin rashes and mucosal lesions respond well to hydroxychloroquine or topical corticosteroids. Mild pleuritis and pericarditis may be treated with NSAIDs. Severe or life-threatening situations, however, including severe pericarditis, hemolytic anemia, thrombocytopenia, renal and CNS involvement may require corticosteroids. Steroid use varies depending on the problem with moderate to high dosages usually given once daily. With serious hematologic disease, more frequent dosing (every 6 hours) is needed. Lupus nephritis, lupus cerebritis, severe vasculitis, and thrombocytopenia frequently require cyclophosphamide as well. The latter classes of patients must be extremely closely monitored for adverse effects and superimposed infections. A major source of mortality in SLE patients is infectious complications from the medications. Patients

treated with corticosteroids also have accelerated atherosclerotic disease with an increased risk of myocardial infarction. Newer treatments focus on specific components of the immune system and are still under investigation.

SYSTEMIC SCLEROSIS (SS)

Progressive and limited scleroderma may be thought of as a continuum of disease processes. Formerly known as CREST, limited systemic sclerosis (LSS) may indeed, over 15 to 20 years, resemble progressive or diffuse scleroderma. The rapidity and aggressiveness of progressive systemic sclerosis (PSS) is what ignites the devastation and poor prognosis. The hallmarks of PSS and LSS include fibrotic skin thickening, active inflammation, microvascular disease, and immunologic abnormalities. Ninety percent of patients with a form of (SS) have RP. It usually antedates PSS only briefly but may antedate LSS by decades.

SS has a female predominance, with rare occurrences before age 25. It is most common in the 40 to 50 age range and in those of African descent. Occupational and environmental risk factors include exposure to silica dust, employment as stone masons, coal miners, dry cleaners, and epoxy resin manufacturers.

LSS is defined as limited skin involvement with the proximal limits of skin thickening at the wrists and ankles. Patients may also have calcinosis, which is deposits of hydroxy apatite (HA) particles in the muscles and soft tissues. These may become quite large and interfere with function or drain and become a risk for secondary infection. The serum calcium in these cases is normal, and no therapy adequately removes these deposits.

Esophageal dysmotility is also problematic with LSS due to relaxation of the lower esophageal sphincter and involvement of the smooth muscles in the lower two-thirds of the esophagus. Raising the head of the bed, histamine 2 antagonists, or prokinetic medications may be helpful symptomatically. The RP, which may have been present for decades, is best treated with avoidance to cold and the therapies outlined above. The calcium channel blockers, however, may exacerbate any esophageal dysmotility problems. Telangiectasias may be present anywhere on the body including the mucosal surfaces. These are seen in both PSS and LSS. Some forms of scleroderma are truly localized to the skin and include patches of sclerodermatous skin called morphea and

linear scleroderma, which presents with linear streaks or bands of scleroderma skin changes. The most severe early change that may be seen in LSS is the isolated pulmonary hypertension. These individuals develop rapid onset dyspnea, and despite vasodilator treatment the prognosis is poor.

Patients with the rapidly progressing skin changes of PSS are at greater risk to develop early and severe visceral involvement. The initial skin changes are those of puffy hands progressively evolving into the indurated skin of scleroderma. Cutaneous sclerosis may involve the extremities, trunk, and face. The skin may take on changes of hyper- or hypopigmentation, become shiny and tight. Friction rubs may be auscultated over tendons. Flexion contractures, skin atrophy, ulceration, and ischemia may ensue. Calcific deposits may occur around the joints, and osteolysis secondary to hypovascularity can cause bone resorption. A mildly inflammatory myopathy may accompany PSS. The gastrointestinal involvement is similar to that of LSS, with additional problems of malabsorption and episodes of pseudoobstruction. These may be quite painful. Atrophy of the walls of the intestine are also a set-up for pneumatosis intestinalis, in which air dissects the bowel wall. Conservative therapy, rather than surgical, is the best approach in these cases. The classic wide mouth diverticula also develop as a result of patchy atrophy of the smooth muscle of the intestinal tract.

The lung involvement most commonly consists of diffuse bibasilar nodular or linear infiltrates and decreased diffusion capacity along with restrictive lung disease. Renal involvement in scleroderma may be lethal. Proteinuria, azotemia, or malignant hypertension may be found in 45% of individuals with PSS. Since the use of ACE inhibitors, however, the mortality has not been as high. The scleroderma renal crisis is acute malignant arterial hypertension, with hyperreninemia and oliguric acute renal failure. There is not much warning of this event, but clues to search for and act upon immediately include small amounts of proteinuria and hematuria. Normotensive renal crisis may present in the patient recently treated with corticosteroids and have accompanying microangiopathic hemolytic anemia and thrombocytopenia.

The diagnosis is best based on the clinical features. Laboratory assessment is not helpful. Antinuclear antibodies are found in most cases. The ANA most commonly has a nucleolar pattern. Anti-SCL70 correlates with PSS and the anticentromere with LSS.

These again are supportive and not to be routine diagnostic tests. In a patient with suspected SS, pulmonary function testing is important to evaluate the DLCO (diffusion capacity). Urinalysis, peripheral blood smear, esophageal imaging, and close monitoring of the blood pressure may aid in detecting any crises early.

The treatment of scleroderma is challenging and to date disappointing and involves symptomatic and supportive measures; nonsteroidal antiinflammatory drugs (NSAIDs); influenza and pneumonia vaccinations; ace inhibitors to protect renal function; antirheumatologic, and antimetabolic measures.

INFLAMMATORY MYOPATHIES

The hallmark of the inflammatory myopathies is proximal muscle weakness with or without associated muscle pain. Patients classically note difficulty raising the arms to fix hair, shave, or brush teeth. Patients also have difficulty getting up from a chair or commode and walking on stairs or an incline. Severe cases may affect the neck muscles, and the head may feel heavy, or there may be problems raising the head from a pillow, chewing, or swallowing. The voice may become more nasal in quality, proximal dysphagia occurs, and food may be regurgitated through the nose. Weight loss may be significant.

In primary adult idiopathic polymyositis (PM), the muscle weakness usually occurs insidiously but may be more acute in onset and may have a relapsing and remitting course. The degree of weakness may vary. Four percent, however, present with respiratory muscle weakness. Patients must be evaluated immediately for the degree and distribution of muscle weakness and functional capacity. If a skin rash is present, the diagnosis of dermatomyositis (DM) (see below) must be considered. Some patients have pulmonary symptoms before the clinically evident myopathy. They may have dyspnea, cough, or hypoventilation secondary to weakness of the respiratory muscles, infectious agents, aspiration, or drug hypersensitivity. Physical examination (PE_x) in these patients will reveal fine crepitant rales, and chest radiographs show fibrosis or a honeycomb pattern. Secondary cor-pulmonale may ensue. The pulmonary function tests reveal a restrictive pattern, reduction in total lung capacity and a moderate reduction in diffusing capacity if fibrosis is present. Joint involvement without overt synovitis may occur during periods of active disease.

Elevations of the creatine phosphokinase (CPK) in the proper setting suggest inflammatory myositis and may be followed during the course of the disease. On occasion it may be massively elevated up to 80 times the normal. On rare instances it is normal; there is no correlation with the degree of elevation and severity of disease. The muscle enzymes including SGOT, LDH, and aldolase also parallel, in their elevated levels, the disease activity. In some patients elevation of LDH or SGOT may be predominant. The latter is often mistaken for hepatic dysfunction. These enzymes, however, may be elevated in other disease states such as hypokalemic periodic paralysis, parasitic infections, drug-induced myopathies, neuromuscular, and metabolic diseases. The sedimentation rate, although not diagnostic, is elevated and may help in following disease fluctuations. In acute PM, myoglobinuria may be present. Associated autoantibodies, again not diagnostic but supportive of the disease, may include a positive ANA and specifically an anti-Jo1 or other antisynthetases, which correlate with pulmonary involvement.

Electromyography (EMG) will show the characteristic small amplitude, short duration, polyphasic motor unit potentials. The EMG should only be done unilaterally so that it may guide the muscle biopsy of the most affected muscle on the opposite side. If a muscle biopsy is done on the side in which the EMG electrodes were placed, there may already be damage from the EMG and the results will not be clear.

Muscle biopsy, without exception, is the means by which to definitively establish the diagnosis. Open surgical biopsy in experienced hands is most important when obtaining muscle tissue. Needle biopsies are not acceptable. The tissue must be handled properly and sent to pathology for full staining and evaluation including enzyme studies and electron microscopy. Many conditions such as enzyme disorders, deposition diseases, and inclusion body myopathy may not be distinguished from idiopathic PM unless muscle tissue is obtained and properly evaluated. Treatment is dependent on a correct and accurate diagnosis. Tissue findings in PM include interstitial infiltrates of inflammatory cells (lymphocytes and macrophages) surrounding and between muscle fibers and small blood vessels. The muscle cells show features of degeneration and regeneration with variation of fiber size and some centralization of nuclei.

Once the diagnosis is suspected or established, a vital capacity should be measured as a baseline for later comparison of pos-

sible diaphragmatic involvement, which may be insidious but life-threatening.

The differential diagnosis of PM is extensive but must be considered before treating as idiopathic inflammatory myopathy and includes denervating conditions, neuromuscular junction disorders, muscular dystrophies, glycogen storage diseases, disorders of lipid metabolism, infections, focal nodular myositis, eosinophilic myositis, inclusion body myositis, polymyalgia rheumatica, drug-induced and granulomatous myositis. Medications that may cause myositis include D-penicillamine, sulfonamides, penicillin, isoniazid, zidovudine, and azathioprine.

DM in adults is identical in clinical presentation to PM except for an associated rash. The classic skin lesions include a heliotrope rash, Gottron's papules and Gottron's sign. The heliotropic rash involves a violaceous coloring of the upper eyelids often with periorbital edema. There may also be a coexistent photosensitive dusky erythematous eruption of the face in the malar, periorbital, V-neck region, shoulders, and upper back. Gottron's papules are violaceous flat plaques of the dorsal aspect of the interphalangeal joints. This may develop into central atrophy with telangiectasia and hypopigmentation. Gottron's sign is more common and is an erythematous, smooth or scaly patch over the dorsal interphalangeal or metacarpophalangeal joints, elbow, knees, and medial malleoli. There may be an associated erythema over the extensor tendons of the hands and forearms. Cutaneous vasculitis presenting as tender nodules, periungual infarctions and digital ulcerations may be seen commonly and is associated with an underlying malignant process. The nail folds may be hyperemic with telangiectasias, ectatic capillaries, and cuticular overgrowth. Calcinosis may be a prominent feature of DM, particularly in children. Vascular involvement, perifascicular atrophy, and perivascular infiltration is seen more often in DM than in polymyositis.

DM has a higher incidence of malignancy associated with it than PM. One-third of patients over 40 with DM have a malignancy preceding, concurrent with or following the diagnosis. In a patient first diagnosed with DM or PM, routine age-appropriate health and cancer screens should be updated. On the other hand, common sense should determine how far to go. A rheumatologist can provide guidelines. Treatment of the malignancy may improve the muscle weakness. Commonly associated malignancies include the lung, breast, ovary, and stomach.

In children, DM is seen more frequently than polymyositis, in boys more than girls. Widespread vasculitis may be seen causing GI hemorrhage and perforation, retinal and macular edema, and visual impairment. The prognosis is actually better than in the adult forms. Calcinosis is more frequent, but there is no association with malignancy.

The initial treatment of both DM and PM is moderate to high-dose corticosteroids until a clinical response is seen and disease remission ensues. Some cases do not require treatment and are self-limited. Laboratory follow-up with serial sedimentation rates and CPK levels are useful. Often the clinical response may lag behind laboratory improvement of the CPK. The corticosteroids are then tapered gradually after 6 to 8 weeks. Corticosteroid sparing agents such as methotrexate and azathioprine may be necessary for those with corticosteroid-dependent disease. Children may do well with pulse therapy of 1 to 2 mg/kg/day of prednisone as may patients who do not respond to oral treatment. Because of the devastating and likely complications of corticosteroids, therapy should be monitored very closely, balancing disease activity and the minimal corticosteroid dose allowable. A point of confusion may be the patient who has been on long-term corticosteroids and suddenly develops muscle weakness again. Although this may be a disease flare, it may well be the presentation of a steroid-induced myopathy. Careful clinical and laboratory assessment may sort this out, but usually failure of response with increases in the corticosteroid doses and improvement after lowering the corticosteroid dose will favor the drug-induced myopathy. Pulmonary and swallowing function should be followed carefully as well.

SJOGREN'S SYNDROME (SJS)

SjS encompasses the clinical manifestations of diminished lacrimal and salivary gland secretions—keratoconjunctivitis sicca and xerostomia. Although SjS is often secondary, accompanying many autoimmune conditions, a primary form also exists. Occasionally this disease may progress to involve extra glandular organs such as the lungs, kidneys, blood vessels, and even develop into a B-cell lymphoproliferative disorder.

The clinical presentations may include complaints of dry and gritty eyes. The development of painful conjunctivitis, pruritus,

discharge, decreased tearing, and sensitivity to light is common. While patients complain of tearing, the tears are reduced in amount and are qualitatively less viscous. The Schirmer test *is done with a standard filter paper placed in the palpebral subconjunctivae while the distance of wetness is quantified*, measures tear flow and can be used to assess decreased lacrimation. Slit lamp examination with Rose Bengal staining is more accurate to evaluate the amount of corneal and scleral epithelial damage.

Patients with the xerostomia complain of a dry and sticky mouth. They often carry their own water around and know where the water fountains are located at work or in shopping centers. They have pain with an associated burning sensation in the mouth and it is difficult to chew and swallow. Taste and speech may be affected and an increase in dental caries is also seen. PEx reveals lack of saliva pool sublingually and parotid gland enlargement. Salivary blood flow may be measured via sialography, but the definitive finding is a minor salivary gland lip biopsy revealing clusters of lymphocytic infiltrates replacing acinar tissue. Occasionally patients may have decreased upper and lower respiratory secretions and develop xerotrachea.

Extra-glandular involvement is present in more than half the patients who present with primary SjS if followed long term, but this is less likely in those with secondary disease. Interstitial lung disease, interstitial nephritis, and renal tubular acidosis may be found in these patients. Vasculitis resulting in palpable purpura and major organ system involvement may also occur. The lymphomas associated with SjS are primarily B-cell origin and may appear after many years of benign disease. This should be suspected in a patient in whom a salivary gland becomes particularly enlarged or firm. Laboratory assessment of SjS will likely reveal a positive ANA, RF (rheumatoid factor), SSA and/or SSB (SjS antibodies A and B), and polyclonal hypergammaglobulinemia.

Other conditions to be considered with bilateral parotid gland enlargement and/ or dry eyes and mouth include bacterial or viral parotitis, HIV disease, amyloidosis, sarcoidosis, chronic pancreatitis, and anticholinergic medications. Serology may help to distinguish the above diagnostic possibilities but biopsy is definitive if necessary.

Treatment of SjS is focused primarily on relief of symptoms and preventing damage as result of the paucity of saliva and tears. Artificial tears used generously may be necessary for relief of the

dry eyes. Careful evaluations of concurrent medications that may cause exacerbation of the dry condition, such as anticholinergics, diuretics, and antidepressants, should be avoided. Frequent ingestion of fluids, especially with meals, is the most prudent recommendation. There is artificial saliva available, which is occasionally effective. Corticosteroid use is reserved for the extra-glandular manifestations such as vasculitis. Hydroxychloroquine and cytotoxic agents may be used. Regular aggressive dental prophylaxis and ocular evaluations are requisite.

UNDIFFERENTIATED CONNECTIVE TISSUE SYNDROMES (UCTD)

The term *mixed connective tissue disease* is reserved for two or more CTDs that are fully expressed in a given individual in association with high antibody titers to the ribonucleic protein (anti-RNP). The others are termed overlap or UCTD. Treatment is based on the symptoms of their dominant diseases and discussed under each specific illness.

AN APPROACH TO VASCULITIS

Vasculitis, defined as inflammation of a blood vessel covers many clinical syndromes and diseases. Vasculitis represents a systemic illness and is manifest with multiorgan involvement, fever, and associated constitutional symptoms. Before the diagnosis of vasculitis is considered, underlying infection, often atypical or disseminated, must be ruled out. TB, hepatitis, and SBE are common infections that may mimic or be the source of the vasculitis. Diagnosis of the infection may require invasive tissue sampling and culture such as bone marrow or liver biopsy. Treatment of the infectious etiology is paramount since treatment aimed at systemic vasculitis involves extensive immunosuppression, and if the infection is not sought or treated, it could worsen and cause the ultimate patient demise. Equally important in the evaluation of a patient with vasculitis is the determination of the organ systems involved. Stool test for occult blood will help in determining GI involvement, and a routine urinalysis searching for blood, casts, and protein may help discover renal involvement. Liver function tests may also detect hepatic involvement. Careful examination of the skin, cuticles and fingernails along with mucous membranes may reveal clues. A classic lacelike rash of livido reticularis is often a clue to underlying vasculitis.

There are two main approaches to the various types of vasculitis. One is based on the involved vessel size (small, medium, or large vessel) and the associated clinical scenario, and the other is based upon the pathologic classification of either allergic, granulomatous, or necrotizing vasculitis. Neither is encompassing and often a combination of the two approaches is necessary to focus on a diagnosis. The clinical scenario and history along with pattern recognition of organ involvement usually lead to the proper diagnosis. However, biopsy and careful pathologic examination of the tissue of the involved organs are necessary for documentation in the classic as well as nonclassic presentations. A brief overview of the various vasculitic syndromes and the pathologic considerations will follow. When a true vasculitis is suspected, prompt diagnosis and treatment are essential since these diseases may blossom rapidly, and most are fatal if not caught and treated early.

SMALL VESSEL VASCULITIS (SVV)

An SVV usually involves the skin, synovium, and GI tract. There may also be rare involvement of kidneys, CNS, and eyes. Hypersensitivity vasculitis occurs secondary to an immune response to an exogenous stimulus such as medications. The clinical onset of arthritis and palpable purpura is usually rapid. Pathologic evaluation reveals leukocytoclastic vasculitis, and laboratory may reveal decreased complement and eosinophilia. Henoch Schoenlein purpura (HSP) is another SVV that usually evolves after a respiratory infection in young children. Patients develop palpable purpura of the lower extremities, hematuria, and GI bleeding. HSP usually resolves spontaneously within 2 to 3 weeks, and no therapy is needed unless there is significant GI involvement. Elevated IgA levels are seen. Behçet's syndrome most commonly involves the small arteries, although there may be rare involvement of the larger vessels. Behçet's syndrome is a vasculitis often in those of Eastern Mediterranean or Far East background. Criteria for Behçet's syndrome include three or more attacks per year of recurrent aphthous oral ulcers along with genital aphthous ulcers, and inflammation of the eye and skin. Later involvement includes erythema nodosum, pseudofolliculitis, or papular pustular lesions, and a positive pathergy test (for exhibition of positivity on skin testing with any antigen in response to mechanical trauma only). The CNS involvement may also be affected, and

synovitis and major vessel occlusion and/or aneurysms may occur. A major and often difficult diagnostic possibility in patients in whom Bechet's syndrome is considered is Crohn's disease, in which an intestinal biopsy may help.

MEDIUM VESSEL VASCULITIS (MVV)

With vasculitic involvement of the medium-sized vessels, there may be overlap with involvement of some of the smaller vessels as well. The clinical presentation of an MVV may therefore have many features in common with the small vessel vasculitis, including the skin and joint involvement, but renal, gastrointestinal, cardiac, and pulmonary involvement is seen as well. The vasculitis of SLE falls into this category. Polyarteritis nodosa (PAN) is another systemic vasculitis that must be considered when there is clinical evidence of GI, renal, cardiac, and skin involvement. Patients with PAN may also have peripheral nerve involvement due to a vasculopathic process occurring in the vasovasorum of the nerves. If there is peripheral nerve, skin, or testicular involvement, biopsy of the involved area may be diagnostic. If there is no such superficial involvement and abdominal pain, a mesenteric arteriogram will reveal the classic beading or aneurysmal dilatation of the involved vasculature. Ultimately, tissue biopsy of the involved organ is necessary. A prompt and organized investigation under the guidance of a rheumatologist is essential for reducing mortality.

Allergic granulomatosis and angiitis, Churg-Strauss syndrome, is a distinctive medium-vessel vasculitis in patients with a history of asthma and/or allergy. Eosinophilia will accompany the clinical presentation. Along with the above triad, there may be systemic illness such as fever, weight loss and malaise. Biopsy reveals angiitis and extramural necrotizing microgranulomas. The major differential diagnosis in suspected Churg-Strauss is Loeffler's syndrome, hypersensitivity vasculitis and Wegener's granulomatosis (WG).

WG is a triad of necrotizing granulomatous vasculitis of the upper respiratory tract (sinuses), lower respiratory tract, and kidneys. In some cases of WG only focal involvement of lungs or kidneys is seen. Fever, malaise, weight loss, arthralgias, myalgia, and worsening sinusitis are common symptoms. Mucosal ulcerations of the nose, hemoptysis, and epistaxis are classic presenting features of WG. Proteinuria, hematuria, and red cell casts on UA should be

quantified and are associated with the renal involvement of WG. C-ANCA (cytoplasmic antineutrophilic cytoplasmic antibodies) may help support the diagnosis but as with any laboratory test does not make the diagnosis by itself. C-ANCA may also help in following the disease course. A biopsy of involved tissue is again most important in making the diagnosis. However, a lung biopsy has the highest yield. Septic processes, especially fungal and mycobacterial infections, must be excluded. Treatment requires careful use of cyclophosphamide with or without corticosteroids.

LARGE VESSEL VASCULITIS (LVV)

Takayasu arteritis (“pulseless disease”) affects young women primarily of Asian and Hispanic descent and involves the aorta. The hallmark of vascular insufficiency and difficulty in detecting pulses or blood pressure may be antedated by synovitis, erythema nodosum, and constitutional symptoms. Claudication, angina pectoris, headaches, and cool extremities are clues of vascular compromise. Patients usually have blood pressure and pulse discrepancies when both sides of the body are compared, and arterial bruits may be auscultated. Some are hypertensive because of renal artery stenosis. The diagnosis is confirmed by arteriogram, and because of the size of the arteries involved, a biopsy is rarely obtained.

Temporal arteritis (TA) and polymyalgia rheumatica (PMR) comprise a spectrum of the LVV commonly occurring in individuals over age 50. TA classically manifests itself as headache, tenderness over the scalp in the area of the temporal artery, jaw claudication, and visual disturbances. The laboratory assessment may reveal anemia and a very high sedimentation rate. Unfortunately not all cases are classic, and the symptoms of atherosclerotic disease and TA may overlap. It is crucial, therefore, to biopsy the temporal arteries to establish the granulomatous infiltration of the intimal layer of vessel wall. Because the infiltration may be patchy, a large section (2 to 3 cm) of artery need be removed and bilateral biopsies will increase the yield. The treatment is covered in Chapter 3.

Patients with PMR complain of muscle tenderness, achiness, and a feeling of weakness of the proximal muscles. The distinguishing feature setting this apart from PM is that these patients have normal muscle strength. The CPKs are also normal, but the sedimentation rate is elevated. Diagnosis is based on the clinical

Table 27.2.
Connective tissue diseases-selected findings.

	Laboratory	Raynaud's/ Muscle	Skin	Vasculitis	GI	Heart/Lung	Kidney
Raynaud's	+ANA common	+ + + + / -	Digital ulcers	+ / -	Esophagus lower 2/3	+ / - angina	-
SLE	Hematologic abnormalities +ANA, +anti- DNA +anti-Sm, Ro, urine: protein and cells/casts	+ + / -	Discoid, malar rash, livedo reticularis	+ + Varies	Unusual	Pericarditis pleuritis, pulmonary infiltrates, vascular changes	Glomerulonephritis
Systemic sclerosis	Nucleolar ANA SCL-70 Anti-centromere (CREST) Decreased diffusion capacity	+ + + + +	Scleroderma	+ +	Esophagus lower 2/3, large diverticula malabsorption/ stasis	Pulmonary fibrosis, cor pulmonale	Severe malignant HTN
Inflammatory myopathy	ANA + / - , +EMG/muscle biopsy, elevated CPK, aldolase, ALT, LDH	- / + + + +	Dermatomyositis Gottron's papules heliotrope facial/truncal	+ / -	Esophagus upper 1/3, aspiration	Pulmonary fibrosis, cardiac myopathy	-
Sjogren's syndrome	ANA + , +SSA/SSB, RF+	- / -	-	- / Rare	Sicca, dry eyes/mouth	Rare	Tubular acidosis

**Table 27.2 (continued).
Connective tissue diseases-selected findings.**

	Laboratory	Raynaud's/ Muscle	Skin	Vasculitis	GI	Heart/Lung	Kidney
Undifferentiated CTD	Many +ANA + RNP	+/+	+	+	+	+	+
Small vessel vasculitis	+ ANCA (P) increased IgA	-/-	++	+++	Vasculitis	-	Vasculitis
Polyarthritis	+ Hep B + ANCA (P)	+/-, -	++	+++ Medium vessels	Vasculitis	Cardiac vasculitis	+++ Glomerulonephritis
Wegener's granulomatosis	+ ANCA (C)	-/-	Vasculitis	Necrotizing granuloma	-	Pulmonary vasculitis, sinusitis	Granulomatous glomerulonephritis
Temporal arteritis	Elevated sedimentation rate	-/+ (PMR)	-	Large vessel/ cranial, other	Rare vasculitis	Rare	-

and laboratory assessment. These patients are treated with much lower corticosteroid doses of 15 to 20 mg daily. It is extremely important, however, to be aware that these conditions may coexist and overlap. The patient with TA may have symptoms of PMR, but more serious is the PMR patient who develops symptoms of TA, since he or she is at risk for blindness and stroke. Frequent and careful questioning is important in picking up the clinical clues and making the proper diagnosis at different times in the course of disease. Treatment of TA should begin promptly without waiting for the confirmatory biopsy, since waiting may lead to sudden and irreversible loss of vision.

CONCLUSION

The most essential component in accurate diagnosis and treatment is the PEx. After all the findings are obtained, it is then necessary to attempt to place these finding in a diagnostic category (Table 27.2). Not all patients fit neatly into one symptom complex and may need to be followed and re-evaluated over time. While the laboratory assessment may be supportive, it is never diagnostic and should be used cautiously. Because of the rarity and complexity of these illnesses, rheumatologic consultation is often recommended. The treatment and prognosis, often the patient's life, depends on an accurate and precise diagnosis, made in a timely manner.

References

1. Schumacher HR, Klippel JH, Koopman WJ. Primer on the rheumatic diseases. Atlanta: Arthritis Foundation, 1993.

Suggested Reading

Schumacher HR, Klippel JH, Koopman WJ. Primer on the rheumatic diseases. Atlanta: Arthritis Foundation, 1993.

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Sports Medicine

Chapter 28

Sports Medicine

John A. Lombardo

Sports medicine can be defined as the care of the physically active and the use of physical activity in the care of the patient. The practice of sports medicine began as an application of medical knowledge and expertise to the specific situations and needs of competitive athletes. Presently, the knowledge that has been gained through the care of competitive athletes is being applied to the general populace. The various patient populations can be described as follows:

1. Competitive athlete—athlete who competes on an inter-scholastic, intercollegiate, professional, or elite amateur team
2. Competitive-recreational athlete—athlete who competes on an organized team with scheduled events or contests
3. Recreational athlete—athlete who enjoys physical activity that is an integral part of her/his life but does not compete regularly
4. Occupational athlete—athlete whose job requires physical activity or exertion
5. Potential athlete—athlete who has either stopped regular physical activity or who has never had physical activity as an integral part of her/his life

The goal of this chapter is to present some of the terms and topics that are specific to the field of sports medicine and to provide reference data to support the primary-care physician in a part-time sports medicine role.

HEALTHY LIFESTYLE

A healthy lifestyle is one that places a high priority on factors of diet, exercise, sleep, relaxation, purity, and balance, all of which are all in the control of the individual. Optimal performance in life is no different than optimal performance in a sporting event. Both take preparation, commitment, and consistency to reach a well-defined goal. Exercise physiology is addressed quantitatively in Chapter 40.

PREPARTICIPATION EVALUATION

The preparticipation evaluation should be performed by a physician who assumes responsibility for the clearance of the athlete. Minimal requirements for this responsibility should include an M.D. or D.O. degree and legal license. Portions of the examination can be performed by other health care professionals, but clearance should be given by a licensed physician. The evaluation is preferably performed 6 weeks prior to the beginning of the season. Logistics may dictate that the evaluation be performed earlier or later. If there is continuity of care for the athlete and the state statutes do not dictate otherwise, an entry-level full evaluation with annual history and limited physical can be sufficient. Based upon the health care environment, physician familiarity, and interest in sports and availability of appointments, an office evaluation or station-based screening evaluation can be used. Routine screening tests have not been shown to be medically indicated nor cost and time efficient.

The main objective is the identification of conditions that will place the athlete at risk of exacerbation of an existing illness or injury or incurring a new problem (the most catastrophic of all conditions being sudden death). The other objectives include determination of general health of the athlete, assessing fitness level, counseling the athlete as to health care concerns for her/his age group, and fulfillment of legal and insurance needs. Table 28.1 provides guideposts for specific organ and physiologic systems according to degree of contact anticipated. Table 28.2 categorizes the common sports by degree of contact.

Table 28.1. Recommendations for participation in competitive sports.

Consideration in Patient	Contact			Noncontact	
	Contact/ Collision	Limited Contact/ Collision	Strenuous	Moderately Strenuous	Nonstrenuous
<i>Atlantoaxial instability</i>	No	No	Yes ^a	Yes	Yes
<i>Acute illnesses</i>	b	b	b	b	b
<i>Cardiovascular system</i>	No	No	No	No	No
<i>Carditis</i>					
<i>Hypertension</i>	Yes	Yes	Yes	Yes	Yes
<i>Mild</i>	c	c	c	c	c
<i>Moderate</i>	c	c	c	c	c
<i>Severe</i>	d	d	d	d	d
<i>Congenital heart disease</i>					
<i>Eyes</i>					
<i>Absence or loss of function of one eye</i>	e	e	e	e	e
<i>Detached retina</i>	f	f	f	f	f
<i>Inguinal hernia</i>	Yes	Yes	Yes	Yes	Yes
<i>Kidney (absence of one)</i>	No	Yes	Yes	Yes	Yes
<i>Liver (enlarged)</i>	No	No	Yes	Yes	Yes
<i>Musculoskeletal disorders</i>	c	c	c	c	c
<i>Neurologic entities</i>					
<i>History of serious head or spine trauma, repeated concussions or craniotomy</i>	c	c	Yes	Yes	Yes
<i>Convulsive disorder</i>					
<i>Well controlled</i>	Yes	Yes	Yes	Yes	Yes
<i>Poorly controlled</i>	No	No	Yes ^j	Yes	Yes ^h

Table 28.1 (continued).
Recommendations for participation in competitive sports.

Consideration in Patient	Contact		Noncontact	
	Contact/ Collision	Limited Contact/ Collision	Strenuous	Moderately Strenuous
Ovary (absence of one)	Yes	Yes	Yes	Yes
Respiratory	i	i	i	i
Pulmonary insufficiency	Yes	Yes	Yes	Yes
Asthma	Yes	Yes	Yes	Yes
Sickle cell trait	j	j	Yes	Yes
Skin (boils, herpes, impetigo, scabies)	No	No	No	Yes
Spleen (enlarged)	Yes ^k	Yes ^k	Yes	Yes
Testicle (absent or undescended)				

^aSwimming (no butterfly, breast-stroke, or diving starts).

^bNeeds individual assessment (e.g., contagiousness to others, risk of worsening illness).

^cNeeds individual assessment.

^dPatients with mild forms can be allowed a full range of physical activities; patients with mild or severe forms or who are postoperative should be evaluated by a physician.

^eAvailability of American Society for Testing Materials approved eye guards may allow competitor to participate in most sports, but it must be judged on an individual basis.

^fConsult ophthalmologist.

^gNo swimming or weight lifting.

^hNo archery or riflery.

ⁱMay be allowed to compete if oxygenation remains satisfactory during a graded stress test.

^jNo gymnastics with mats, martial arts, wrestling, or contact sports until no longer contagious.

^kCertain sports may require a protective cup.

Table 28.2.
Classification of sports.

Contact			Noncontact	
Contact/Collision	Limited Contact/Impact		Strenuous	Moderately Strenuous
Boxing	Baseball		Aerobic dance	Badminton
Field hockey	Basketball		Crew	Curling
Football	Bicycling		Fencing	Table tennis
Ice hockey	Diving		Field (discus, javelin, shot)	
Lacrosse	Field (high jump, pole vault)		Running/track	
Martial arts	Gymnastics		Swimming	
Rodeo	Horseback riding		Tennis	
Soccer	Skating		Weight lifting	
Wrestling	Skiing			
	Softball			
	Squash/handball			
	Volleyball			
				Archery
				Golf
				Riflery

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The Preparticipation Physical Evaluation Monograph, which is jointly produced by five organizations, makes suggestions for various aspects of the evaluation (1). This is a reference that is essential to physicians whose patients include interscholastic and intercollegiate athletes.

History

The history reflects the goals and objectives and targets conditions that will impair the ability of the athlete to perform safely the desired activity. The cardiovascular, neurologic, respiratory and musculoskeletal systems, medications, allergies, hospitalizations, surgeries, environmental, skin and eye problems, and equipment needs are extremely important if the goal of the evaluation is to be accomplished. The menstrual history of women athletes should be obtained. The biopsychosocial aspects of the athlete are becoming more prevalent and should be addressed.

Physical

The preparticipation physical examination is a limited one, which evaluates the areas of greatest concern. Vital signs, height and weight, and visual acuity must be available for the physician performing the remainder of the examination. Eyes, ears, nose, throat, heart, peripheral pulses, lungs, abdomen, male genitalia, and skin should be thoroughly evaluated. If the athlete is known to have received a general medical examination within a medically uneventful year, a limited musculoskeletal examination such as the 13-point examination can be performed in certain situations and will supply sufficient information for decisions on clearance (Table 28.3). Another option is a sport-specific examination, such as checking for hepatomegaly and absence of a kidney in a prospective contact/collision athlete, which would be disapproved (Table 28.1). In some sports-specific situations and/or at higher levels of competition, a more complete musculoskeletal examination can and in some instances should be performed.

Clearance

When considering clearance for activity, the physician must remember the goal of the evaluation, the health and safety of the athlete. If the athlete or another participant is at risk of injury, or if the athlete's problem cannot be treated or protected, clearance should

Table 28.3.**Areas covered in the 13-point musculoskeletal examination.**

-
1. Front inspection (e.g., deformities, asymmetries, swellings).
 2. Neck range of motion (ROM).
 3. Trapezius strength.
 4. Upper extremities, abduction, deltoids.
 5. Shoulders ROM—internal, external, rotation—and strength.
 6. Elbows ROM—flexion, extension
 7. Elbows ROM—pronation, supination.
 8. Hands inspections, ROM and strength—interossei lumbricals and wrist flexion, extension.
 9. Rear inspection.
 10. Back flexibility, symmetry.
 11. Lower extremities inspection.
 12. Lower extremities ROM, include squat.
 13. Lower extremities ROM, heel, toe walk.
-

not be given or should be limited. Clearance can be limited to certain activities and is definitely not an “all or none” phenomenon.

Important factors to consider include:

1. General health—acute and/or chronic diseases, general health assessment with an emphasis on neurological problems, musculoskeletal injuries, cardiovascular abnormalities
2. Level of conditioning—specific areas may need to be addressed for various activities (e.g., low back condition prior to golf)
3. Occupational stresses—if physical activity is part of daily routine, could additional activities contribute to overload (overuse) injuries
4. Social history—use of stimulants such as tobacco or caffeine, alcohol and/or illicit drugs
5. Activity experience—if limited previous experience with the activity (e.g., tennis or golf), the instruction in the skills necessary to play may help avoid problems
6. Patient's goals—knowing the reason for the patient's beginning on an exercise program will assist the physician in counseling the patient on the appropriateness of the chosen activity in the attainment of the goals

As physical activity and sports participation increases past the collegiate years, the number of patients requesting assistance in preparation for safe and enjoyable participation in these activities also increases.

CONDITIONING AND TRAINING

There are three main parts to conditioning—flexibility, strength, and endurance. A general conditioning program should include all three parts. If a person wants to participate in a specific sport or activity, the training program needs to be tailored for the demands of that particular activity.

The conditioning program for cardiovascular fitness has been referred to as the “Exercise Prescription.” This can be expanded to include a program designed with general overall conditioning as the goal and include a strength and flexibility component. The five parts of the exercise prescription are:

1. Mode—depending on the area to be conditioned, this may refer to different types of activities:
 - a. Endurance activity
 - b. Exercises such as biking, jogging, swimming, skating, walking, using a “stepper,” rowing that contribute to the development of cardiovascular and muscular endurance
 - c. Strengthening activity
 - d. Isometric, isotonic, isokinetic exercises using free weights, spring-loaded devices, weight machines, elastic bands, electronic devices, or any object with a mass such as a bale of hay or a rock that overloads muscles and/or muscle groups and thereby increases strength
 - e. Flexibility activity
 - f. Exercises that stretch the muscle and/or muscle groups thereby allowing for more fluid motion of joints and less tension on muscles as activities are performed
2. Intensity—the amount of effort that is exerted in the performance of the exercise is the intensity; the “percent of maximum” heart rate, effort or lift defines the intensity of the endurance or strengthening activities
3. Duration—the length of time that an activity is performed; this may refer to distance, number of sets or length of time a stretch is held
4. Frequency—the number of times an activity is performed in a day, week or month
5. Progression—the rate at which a given activity should be progressed; this includes changes in intensity, duration, and frequency

These variables are important not only in the development of an exercise or conditioning program, but also in the transi-

tioning of an injured athlete who is returning to her/his previous level of activity.

OVERUSE INJURIES

Musculoskeletal injuries are the result of a mechanical overload to bone, the muscle-tendon unit, or other connective tissue. Acute injuries are an event and the result of a sudden and large force, which causes macroinjury. The physician should search for the mechanism of injury to better understand and diagnose the problem. Overuse injuries are a process and the result of repetitive smaller forces causing microinjuries.

If the activities of daily living cause continued overload to the injured area, the problem can persist until the cycle is broken. The best option for the patient who wishes to return to activity without problem is to follow the 3 R's: relative rest, rehabilitation, return gradually. Relative rest (to the injured part) may comprise a reduction, change, or cessation of activity. Rehabilitation is the reconditioning of an injured area, to be discussed. Return to activity must be scheduled so that the injured area or another area is not injured by too rapid a return.

The etiology of the overuse injury must be identified if adequate treatment is to be given. The etiologies of overuse injuries include: 1) training errors; too rapid a progression, i.e., intensity, duration, frequency; insufficient level of conditioning, which affects flexibility, strength, endurance; excessive activity; 2) improper mechanics or techniques; 3) improper equipment; 4) environmental factors, e.g., surface factor; pitch and texture; and 5) anatomic variants, which constitute structural problems (includes concurrent injury).

RESPONSE TO INJURY, REHABILITATION AND RETURN TO ACTIVITY

RICE is well recognized as the initial treatment for acute injuries. The goal of the initial RICE treatment is the limitation of further injury, reduction of swelling, and pain control.

- R = Relative rest—decreasing or ceasing activities that load the injured area (may require crutches, brace, cast, sling)
- I = Ice—ice is always used on an injured area after activity
- C = Compression—compression of an injured area can be accomplished by an ace bandage or more effectively with an ace bandage and cast padding

E = Elevation—elevation of injured area above level of heart will decrease swelling

Rehabilitation is the reconditioning of an injured area so that normal function can be resumed. Rehabilitation includes therapeutic exercises (flexibility, strength, endurance) for the injured muscles or muscles about an injured joint or bone, their antagonists and the muscles that function in concert with these muscles in the performance of desired function. The appropriate use of electrical stimulation, ultrasound, cryotherapy, thermal agents, compression therapy, and traction all can contribute to the reconditioning effort. Synchrony of firing is essential for athletic activity. This is retrained through transitional activities that require the muscles to perform the desired function slower and/or under lesser loads. Transition is the movement of the athlete from the therapy area to the playing field. This requires knowledge of the demands of the athlete's chosen activity. Rehabilitation of individual injuries will be discussed in the appropriate treatment sections.

Field Management of Head Injuries

The decision as to when to allow an athlete to return to a contact sport event or practice is a clinical one that takes into account the possibilities of skull fracture, neurologic findings and the athlete's alertness, recall, and well-being. Guidelines that have been approved by all concerned medical organizations appear in Table 28.4. These are seen by most team physicians as quite conservative and by some, overly so, but are appropriate for this purpose.

Neck Injuries in Contact Sports

These should be approached at the time of injury with the rules set forth in trauma life support protocols. Care is taken to ensure neck immobility in the neutral position (neither flexion nor extension) for transport from the field and until a cervical spine x-ray has been accomplished.

DRUG USE IN SPORTS

The area of drugs in sports can be divided into three areas:

1. Therapeutic drugs: anti-inflammatories; analgesics; decongestants; antibiotics

Table 28.4.
Grading concussions in sports and guidelines for return to play.^a

Grading		Guidelines		
Severity	Signs/Symptoms	First Concussion	Second Concussion	Third Concussion
Grade I (mild)	Confusion without amnesia; no loss of consciousness	May return to play if asymptomatic ^d for at least 20 minutes	Terminate contest/practice; may return to play if asymptomatic ^d for at least 1 week	Terminate season may return to play in 3 months if asymptomatic ^d
Grade II (moderate)	Confusion with amnesia ^b ; no loss of consciousness ^c	Terminate contest/practice; may return to play if asymptomatic ^d for at least 1 week	Consider terminating season but may return to play if asymptomatic ^d for 1 month	Terminate season may return to play next season if asymptomatic ^d
Grade III (severe)	Loss of consciousness	Terminate contest/practice and transport to hospital; may return to play 1 month after 2 consecutive asymptomatic ^d weeks; conditioning allowed after 1 asymptomatic ^d week	Terminate season; may return to play next season if asymptomatic ^d	Terminate season strongly discourage return to contact/collision sports

^aThese guidelines are not absolute and therefore should not substitute for the clinical judgment of the examining physician.

^bPosttraumatic amnesia (amnesia for events after the impact) or more severe retrograde amnesia (amnesia for events preceding the impact).

^cSome clinicians include "brief" loss of consciousness in grade II and reserve "prolonged" loss of consciousness for grade III. However, the definitions of "brief" and "prolonged" are not universally accepted.

^dNo headache, confusion, dizziness, impaired orientation, or memory dysfunction during rest or exertion.

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2. Performance enhancers: anabolic agents; stimulants; enhancers of oxygenation; relaxants
3. Mood-altering drugs or drugs of abuse: depressants; stimulants; hallucinogens; opiates

The problem of drug abuse in each of these areas is different, and the programs and role of drug testing needed for each also differ.

Therapeutic drugs that help an athlete pass from the abnormal to the normal state are abused when they are used to mask symptoms and allow play without proper protection for the athlete.

Performance enhancers are coercive drugs. If an athlete gains an advantage by using these drugs, other athletes can feel the need to use drugs to maintain competitiveness. When considering the performance enhancers it is important to examine patterns of use, efficacy, adverse effects, ethics, legality, and drug tests.

The issue of illicit drug use by athletes is one that will forever be present, since it will always be a problem in our society. When approaching the problem of mood altering drugs used for entertainment or escape, it is important to remember that drug use is an avoidable behavior and drug dependency is a treatable disease.

Drug programs must be developed that address the goals set by the leadership of the group covered by the program if they are to be successful. The elements for a successful drug program include:

1. A policy that addresses specific drugs and the rules of conduct regarding them
2. Education of the athletes regarding the policy
3. Testing
 - A. Drug testing serves a number of purposes:
 1. Provide early identification of drug use
 2. Refute denial of use
 3. Deter the use of drugs (when a part of complete program)
 4. Serve as marker of effective therapy
 - B. The time of testing and type of testing is dependent upon the drug use patterns:
 1. Event testing
 - a. Stimulants
 - b. Relaxants
 - c. Enhancers of oxygenation
 - d. If sensitive enough, certain anabolic agents

2. Random testing
 - a. Anabolic agents
 - b. Enhancers of oxygenation
 - c. All mood-altering drugs, if performed within 24 hours of an event; can function as an event test
3. Cause testing dependent upon signs and symptoms of a problem—least effective for all drugs

C. Four stages of the testing process

1. *Collection process* must verify the urine as the athlete's. The most effective is observation from urethra to cup. Temperature testing of urine to strip searches for stored urine are not as effective.
 2. Strict adherence to *chain of custody* regulations is necessary to ensure validity to the program.
 3. The *analysis* of the sample is dependent upon the level of technological advancement in detection of substances and the effects of drugs on other parameters. The laboratory must be certified.
 4. *Review of the results* is the final stage of testing process. The medical review officer must be knowledgeable and maintain absolute integrity to the program for it to be successful. The question that must always be asked is whether the intrusion of the privacy of the individual is surpassed by the common good of the group. If the answer is yes, then an approach should be developed to give the highest degree of success while maintaining consideration of the dignity and schedule of the individual.
4. Discipline—discipline must be fair and equitable for all; the risk imposed by the discipline must be greater than the benefit gained by the athlete.
 5. Evaluation and treatment—medically centered programs must include treatment for the problems related to drug use

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Other Infectious Diseases Encountered in Primary Care

Chapter 29

Adult Acquired Immune Deficiency Syndrome

Michael B. Weinstock and Rob Crane

DESCRIPTION OF DISEASE

Each generation of physicians faces one or more of a succession of epidemics that in some ways serves to define the medical care of that era. For us the sentinel epidemic has become the Acquired Immune Deficiency Syndrome (AIDS). Its infectivity reflects our cultural mores. Our battle with it highlights emerging medical technologies and current shortcomings. There are few illnesses about which we know so much but have so few answers. We understand much of the pathogenesis of the illness and have explicitly defined its modes of transmission. Yet for the foreseeable future, we expect 50,000 otherwise healthy, relatively young Americans to die from this disease every year. In the rest of the

world the toll may be an order of magnitude higher, and no end is in sight.

Pathophysiology of the Human Immunodeficiency Virus (HIV)

The human retrovirus, HIV, exists in its free form as an RNA virus and must undergo a reverse transcription to enable it to be inserted into human DNA. This somewhat complicated reproductive process has been a specific target for most of our anti-HIV drugs but unfortunately also affords the virus an easy route to mutation and eventual drug resistance. HIV has a specific affinity for the CD4 receptor found on a subpopulation of T-lymphocytes and some other cells. These T-4 Helper or CD4 lymphocytes play a critical role in cell-mediated immunity and are often metaphorically referred to as the commanding generals of the immune system.

After initial infection, the virus multiplies rapidly both in peripheral CD4 lymphocytes and in lymph nodes. Once a cell has been infected, its genetic structure is irreversibly altered. It may immediately manufacture HIV or function normally for long periods of time with the virus lying latent in its DNA. Over time with chronic infection and destructive viral multiplication, the number of CD4 lymphocytes declines and cellular immunity wanes. The course of HIV infection is variable. Within 10 years approximately half of those infected will have serious complications in the absence of treatment, but even after a decade, a small percentage of patients (5% to 10%) will have neither an important infection nor laboratory evidence of significant decline in their immune systems.

Unlike most other chronic illnesses, the stage of the illness can be readily estimated by a single laboratory test, the CD4 lymphocyte count. A normal CD4 count has a wide range, but most experts choose 1000 CD4 cells/mm³ as an appropriate average starting point. With initial or acute infection, viral reproduction is rapid, and the individual often experiences mononucleosis-like symptoms of viremia, which include fever, lymphadenopathy, sore throat, fatigue, skin rash, and headache. After this syndrome resolves, the patient enters an asymptomatic phase, which may last many years.

As the immune function diminishes over time, minor infections are often manifested on the skin and mucous membranes. Skin manifestations include seborrheic dermatitis, folliculitis, zoster, molluscum contagiosum, tinea corporis, onychomycosis,

candidal dermatitis, psoriasis, and Kaposi's sarcoma (KS). Mucous membrane manifestations include herpes simplex, human papilloma, condyloma, abnormal pap smears, thrush, and hairy leukoplakia. Because of immune confusion, there are hyper-reactive syndromes such as psoriasis, urticaria and frequent drug reactions. There may be general findings of low-grade fever, night sweats, weight loss, fatigue, and diffuse adenopathy. The end stage of HIV infection is AIDS: defined as a CD4 count below $200/\text{mm}^3$ or a serious opportunistic infection. Figure 29.1 details the course of HIV disease in an average patient.

Modes of Transmission and Risk Groups

HIV is transmitted by transfer of blood or body fluids. Body fluids that are documented to carry sufficient virus include blood, semen, vaginal secretions, cerebrospinal fluid (CSF), synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, and amniotic fluid. Body fluids not considered to be at risk include feces, nasal secretions, sputum, saliva, sweat, tears, urine, and vomitus. The safest policy for health-care workers is to use universal precautions with all body fluids.

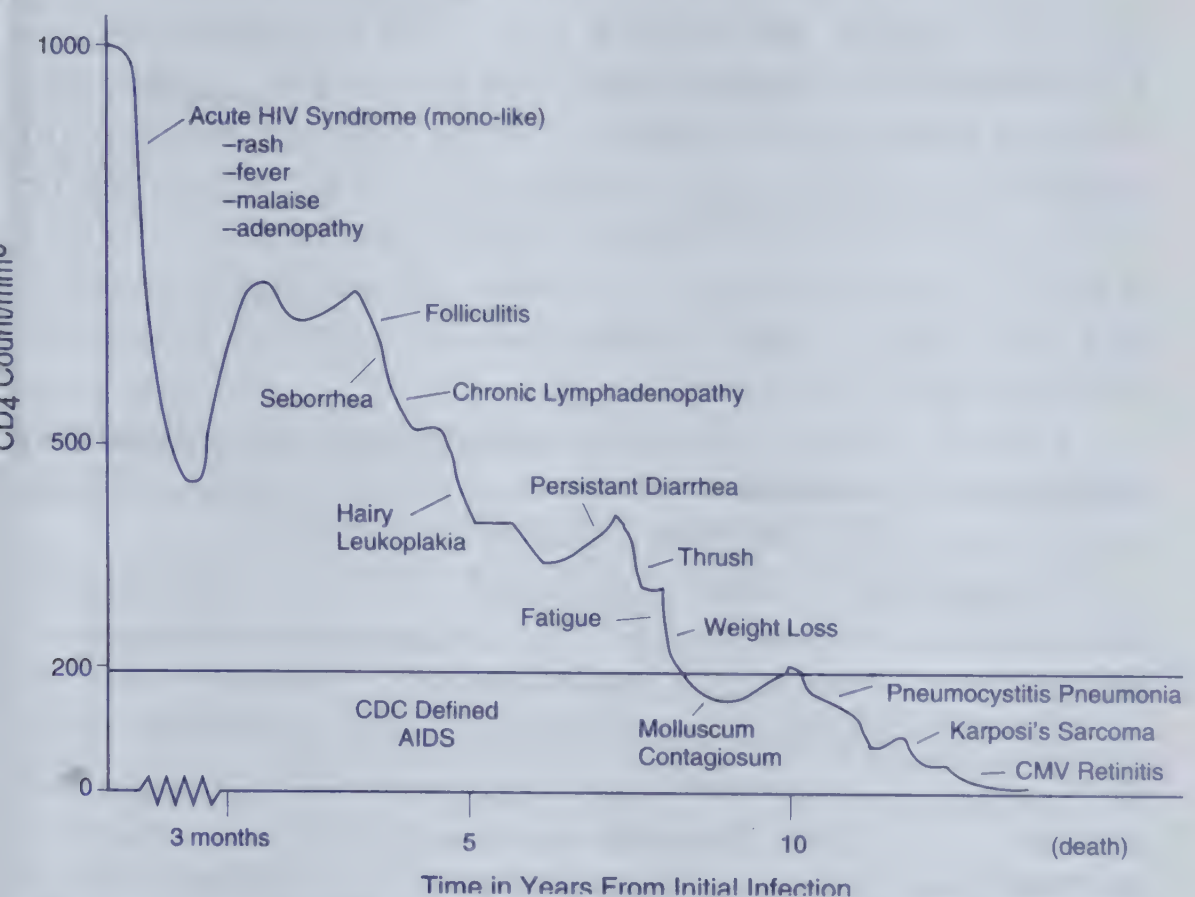


Figure 29.1. "Typical" course of untreated HIV infection. Examples of illnesses that occur at various stages of CD⁴ lymphocyte suppression.

The three groups with the highest prevalence of HIV are gay men, intravenous drug abusers, and hemophiliacs. Wives of hemophiliac men have a rate of 20% to 25%. The rate in prostitutes varies with location and with concomitant intravenous drug use. Other routes of infection include heterosexual transmission and blood transfusions. As of December 1995, all blood is screened for both HIV antibody and antigen. The use of this new technique has decreased the incidence of HIV-infected blood to 1:500,000. Nonintimate contact and household exposure does not increase risk of transmission of HIV.

In 1994, HIV became the leading cause of death in the 25- to 44-year age group. Approximately 12% of patients with HIV convert to AIDS within 5 years of diagnosis and 50% convert at 10 years.

DIAGNOSIS AND CLINICAL COURSE

The diagnosis of infection is usually made by testing for antibodies to HIV. A very sensitive test, the enzyme-linked immunosorbant assay (ELISA or EIA) reacts to several antibodies made in response to viral proteins. If the ELISA is positive, a more specific confirmatory test, the Western Blot, must be performed. The ELISA is 99.5% sensitive if antibodies are present, but may miss infection in the first few weeks or months of the illness before the antibody titer is high. Approximately 97% of individuals will become positive on ELISA testing within 3 months after infection. If there is a question about the results, the test may be repeated at a later date or other confirmatory tests such as polymerase chain reaction (PCR) may be run.

Table 29.1 lists the points upon which to touch in the history and physical examination in patients with HIV. Table 29.2 describes initial testing and vaccinations.

The diagnosis of AIDS is defined by the Centers for Disease Control and Prevention (CDC) as the presence of an opportunistic infection or a CD4 count below 200 /mm³.

The CD4 count is determined by multiplying the WBC count by the percent lymphocytes by the percent CD4 lymphocytes. Anything that affects the white blood cell count may influence the CD4 count (infection, drugs, steroids). If the CD4 count is abnormal, or when therapeutic decisions will be made based on the CD4 count, it should be checked again in 1 to 2 weeks, by the same laboratory. Trends are often more important than actual num-

Table 29.1.
History and physical exam in patients with HIV.

Highlights of History and Physical Examination in Suspected AIDS			
History of Present Illness	Past Medical History	Social History	Physical Examination
Headache/ confusion	Drug allergies	Possible mode of infection	Lymphadenopathy
Fatigue/ weight loss	Hospitalizations	Current sexual practices, drug use, smoking and alcohol use, diet, stressors, support systems	Ophthalmic/ funduscopy exam
Fever/chills/ night sweats	Immunizations		Oral examination
Lymphadenopathy	Medications		Lung and heart exam
Skin changes/ oral lesions	History of infectious diseases especially varicella/zoster, TB, HSV,		Abdominal exam including palpation of liver and spleen
Dysphagia	hepatitis, sexually transmitted diseases	**It is appropriate and important to discuss methods of transmission and which behaviors are threatening to others.	Genital and rectal exam if indicated by history
Change in vision	Recent blood donation		Neurologic exam if indicated by history
Cough/Shortness of breath			Dermatologic exam
Easy bruising			
Nausea/vomiting/diarrhea			
Abdominal pain			
Vaginal/penile discharge			
Yeast infections			
Anal pain			

Table 29.2.
Initial testing and vaccinations.

Initial Evaluation and Listing of Immunizations		
Laboratory	Other tests	Immunizations
CBC with differential and chemistries	Chest radiograph	Pneumococcal vaccine
Syphilis and toxoplasma (IgG) serology	PPD skin testing (positive is >5mm)	Hepatitis B vaccine (if seronegative)
Hepatitis B screen	PAP smear (check every 6 months and if normal twice, then every year)	Influenza vaccine
CD4 count		Hemophilus influenza B (HiB)?
Viral load (HIV-RNA PCR)		Hepatitis A?

bers. The CD4 count and viral load should be checked every 6 months in asymptomatic patients with counts above $500/\text{mm}^3$ and every 3 months in patients with counts below $500/\text{mm}^3$. The % CD4 count stays fairly constant and may be more reliable than the CD4 count.

A new test to monitor the progression of HIV disease and response to antiretroviral therapy is the determination of viral load. In order to ensure consistent results, the same method and same lab should be used. This results routinely vary by 0.5-log (a factor of three), and the interpretation should take this into account. The viral load should be used in conjunction with the CD4 count, to follow progression of disease, to follow efficacy of antiretroviral agents, and to determine prognosis.

Asymptomatic Disease

There are four main strategies to help asymptomatic patients stay healthy. They include prevention and early treatment of complications, slowing the progression of HIV disease, reducing the transmission of HIV, and improvement in the quality of life.

Schedule a lengthy initial office visit and arrange a follow-up visit within 1 to 2 weeks to explain laboratory results and answer questions. Initially, patients may require frequent visits for counseling and education. Asymptomatic patients should be followed every 3 to 6 months. When the CD4 count is less than $500/\text{mm}^3$, consider visits every 3 months. An ophthalmologic examination should be performed every year when CD4 count drops below 50 to $100/\text{mm}^3$.

Patients should be provided with written information on HIV/AIDS, support groups, unsafe and safe sexual and intravenous drug use practices. Sexual practices that do not exchange body fluids are safe for patients to continue. This should be discussed explicitly with the patient. Past contacts should be notified. This does not have to be done on the first visit, but can be deferred until the doctor-patient relationship has been better established. The need for frequent visits and blood tests should be stressed to the patient.

Overwhelming fear and paralyzing denial have been the two psychological factors that have served to characterize, define, and continue this epidemic. Not since leprosy has an illness carried such a significant stigma. Patients frequently lose jobs, housing

friends, family, and intimate relationships. The diagnosis is often kept as a tightly held and often destructive secret. The professional caring for infected individuals or for those at risk must both recognize the depth of emotions surrounding the diagnosis and act aggressively to counsel and support. Often this requires referral for individual or group therapy. Physicians must be prepared to deal with legal issues, homosexuality, substance abuse issues, AIDS support organizations, clinical trials, and hospice.

Symptoms Management

Figure 29.2 outlines the work-up of AIDS complications; Figure 29.3, the evaluation of fever in HIV disease; and Figure 29.4, the evaluation of shortness of breath.

Management of Pneumocystis Carinii Pneumonia (PCP)

P. Carinii, a one-celled yeastlike protozoan, is a classic opportunistic pathogen. More than half of Americans show antibody evidence of previous infection, yet in the absence of immunodeficiency symptomatic infection is virtually never manifested. The risk of PCP rises as the CD4 count drops below 200 to 250. Symptoms of active disease usually include fever, dry cough, dyspnea, and malaise. Chest x-ray is often normal or reveals a bilateral, patchy interstitial infiltrate, though many x-ray patterns can be seen. Many patients with significant illness will be hypoxemic. The diagnosis is usually made by bronchoscopy and bronchoalveolar lavage (BAL), although in some experienced laboratories induced sputum with special stains may be diagnostic (Table 29.3).

Pneumocystitis Carinii Prophylaxis

The first-line medication for PCP prophylaxis is trimethoprim-sulfamethoxazole (Bactrim). It is low cost, has a low relapse rate, and it has activity against toxoplasmosis and legionella in addition to pneumocystis. If it is not tolerated due to rash, GI upset, or fever, a desensitization protocol may be attempted (Tables 29.4, 29.5).

Indications for PCP prophylaxis:

1. Prior PCP
2. $CD4 < 200$ cells/mm³

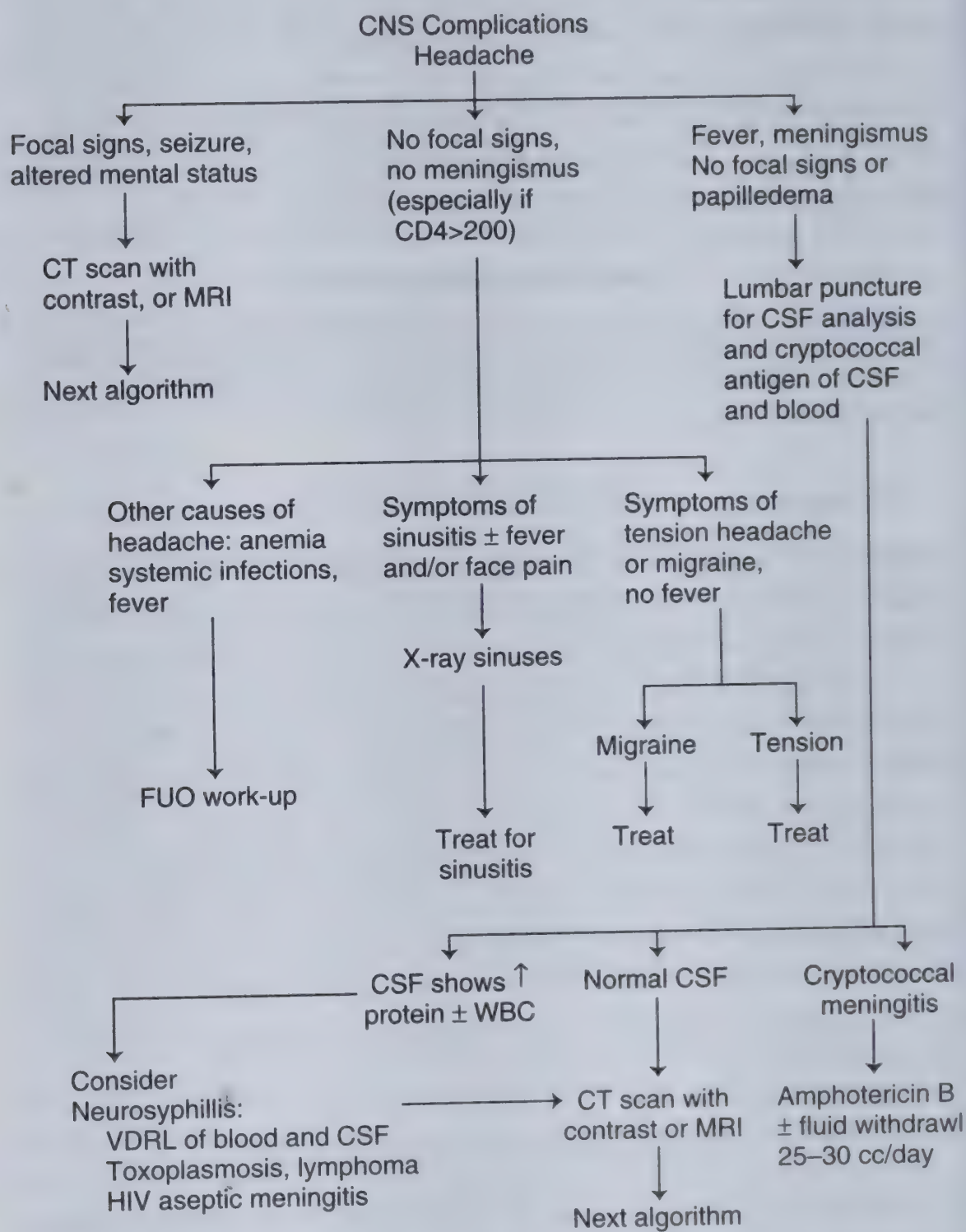


Figure 29.2. Major complications of HIV infection. Headache; CT, computerized tomography; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid; FUO, fever of unknown origin; WBC, white blood cell count; VDRL, venereal disease research laboratory; 5FC, 5-flucytosine. (Reprinted with permission from Bartlett G. The Johns Hopkins Hospital guide to medical care of HIV patients. 6th ed. Baltimore: Williams & Wilkins, 1996.)

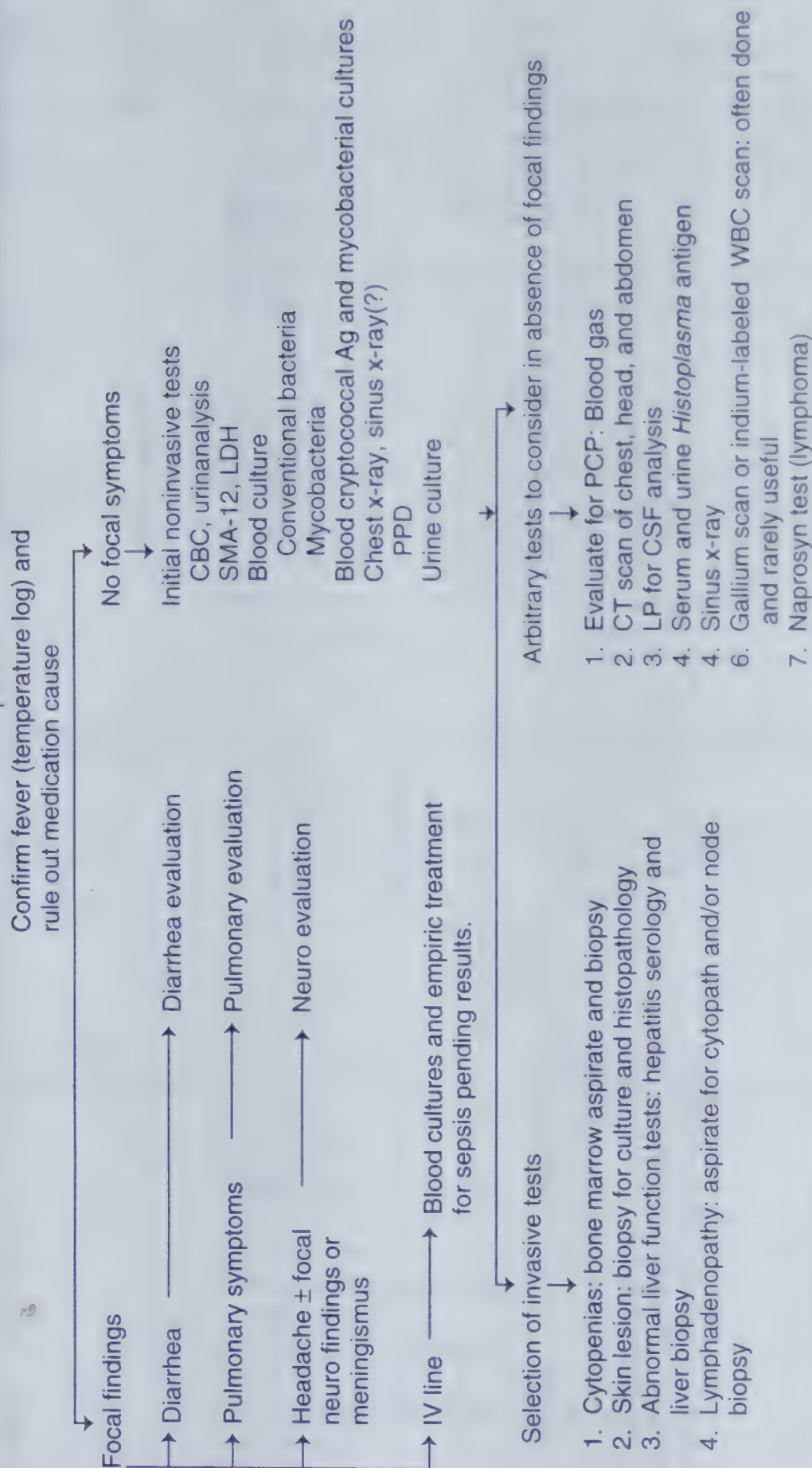


Figure 29.3. Evaluation of fever in HIV disease. FUO, fever of unknown origin. (Reprinted with permission from Bartlett G. The Johns Hopkins Hospital guide to medical care of HIV patients. 6th ed. Baltimore: Williams & Wilkins, 1996.)

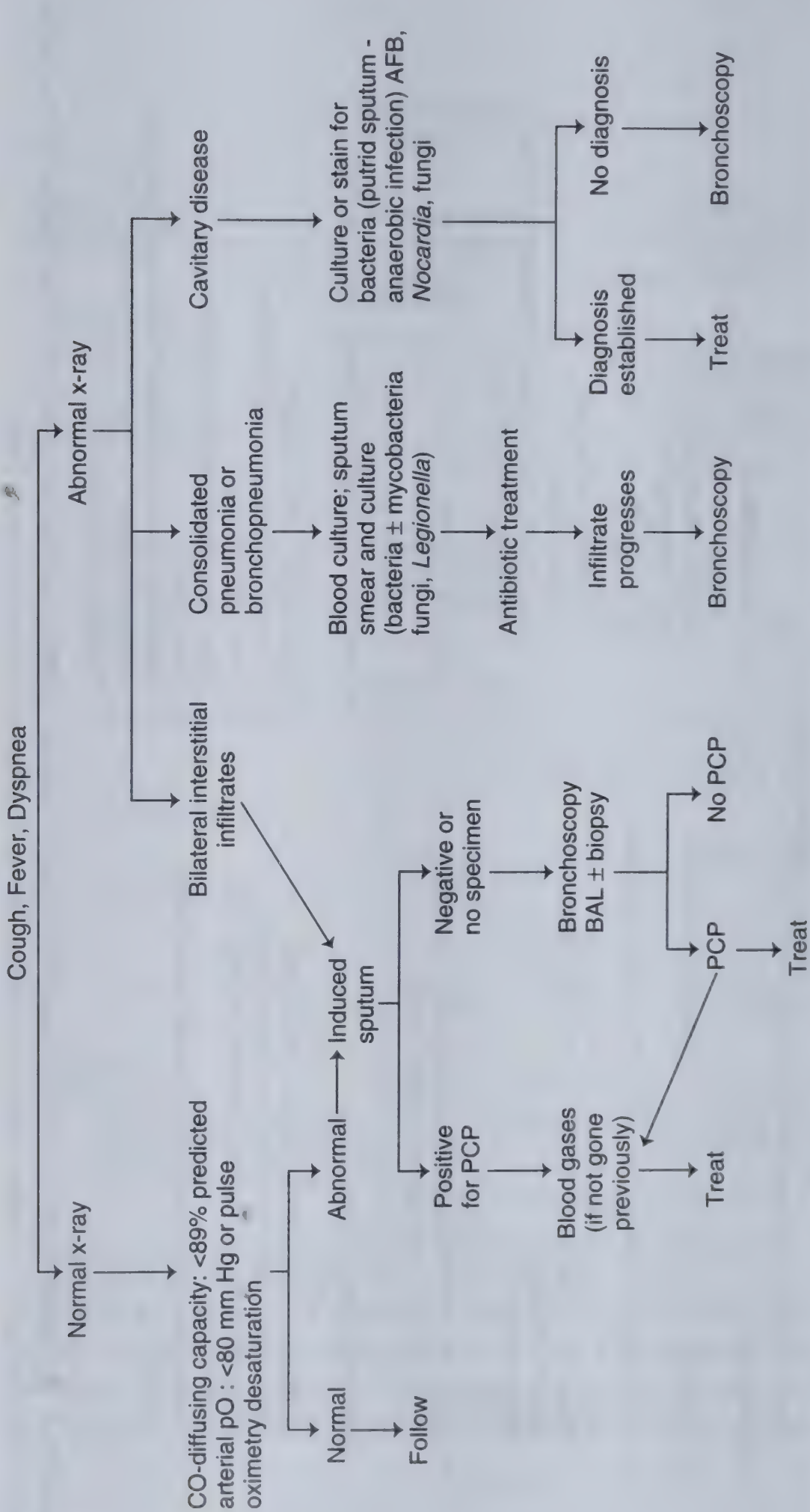


Figure 29.4. Evaluation of shortness of breath. (Reprinted with permission from Bartlett G. The Johns Hopkins Hospital guide to medical care of HIV patients. 6th ed. Baltimore: Williams & Wilkins, 1996.)

Table 29.3.
Treatment of opportunistic infections.

Opportunistic Infections ^a	First Line	Alternative
Pneumocystis carinii pneumonia	Trimethoprim-sulfamethoxazole (TMP/SMX): 15–20 mg/kg (TMP) i.v. or po for 21 days Prednisone taper: if $pO_2 < 70$ mm Hg 40 mg bid \times 5 days, then 40 mg qd \times 5 days, then 20 mg qd \times 11 days	Pentamidine: 3–4 mg/kg i.v. qd for 21 days or Atovaquone-750 mg po tid Prednisone taper: if $pO_2 < 70$ mm Hg (see left)
Toxoplasma encephalitis	Pyrimethamine (Daraprim): 100–200 mg loading dose, then 50–100 mg po qd <i>plus</i> Sulfadiazine: 4–8 g po in divided doses for 6 weeks <i>plus</i> Folinic acid- 10mg qd	Pyrimethamine + clindamycin (Cleocin): 50–100 mg po qd and 450–600 mg po qid respectively for 6 weeks
Cytomegalovirus (CMV) Retinitis	Ganciclovir (Cytovene): 5mg/kg i.v. q 12h for 14–21 days	Foscarnet (Foscavir): 60 mg/kg i.v. q 8h for 14–21 days
Cryptococcal meningitis	Amphotericin B: 0.7–0.8 mg/kg i.v. qd \times 2 weeks, followed by Fluconazole: 400mg qd for the rest of the acute therapy (8–10 weeks)	Fluconazole (Diflucan): 400 mg po for 8–10 weeks
Mycobacterium avium complex	Clarithromycin (Biaxin): 500 mg po bid <i>plus</i> Ethambutol (Myambutol): 15 mg/kg po qd <i>plus one or more of the following</i> Clofazimine (Lamprene): 100 mg po/d Ciprofloxacin (Cipro): 750 mg po bid Rifabutin (Mycobutin): 600 mg qd	Azithromycin (Zithromax): 500 mg po/d

^aAll require chronic suppressive therapy (secondary prophylaxis) after acute treatment.

Table 29.4.
Prophylaxis of pneumocystis carinii pneumonia.

Medication	Dose	Cost/yr.	Relapse Rate	Side Effects
Trimethoprim-sulfamethoxazole	One DS tab qd or TIW	\$15-25	0-5%/year	Rash, nausea/vomiting, fever, anemia, neutropenia, Stevens-Johnson
Dapsone	50-100 mg po qd	\$18-70	5-20%/year	Rash, agranulocytosis, aplastic anemia, hemolytic anemia in G6PD deficiency
Aerosolized pentamidine	300 mg per month administered over 30-45 minutes	\$1,200-1,700 plus cost of administration	15-25%/year	Brochospasm, increased incidence of upper lobe disease and extrapulmonary PCP

Table 29.5.
Prophylaxis of other opportunistic infections.

Opportunistic Infection	Drug	Alternative Medication	Side Effects	Indications
Tuberculosis	Isoniazid (INH) 300 mg qd for 1 year. Consider pyridoxine 50 mg qd	Rifampin 600 mg qd for 1 year	Hepatitis, rash, peripheral neuropathy	PPD > 5 mm or exposure (see text)
MAI/MAC	Clarithromycin (Biaxin) 500 mg bid	Rifabutin (Mycobutin) 300 mg qd	Clarithromycin: GI disturbances Rifabutin: Neutropenia, thrombocytopenia, rash and GI, uveitis	Primary prophylaxis with CD4 < 50–75/mm ³
Cryptococca 1 meningitis	Fluconazole (Diflucan) 200–400 mg qd	Amphotericin B: 0.5–1 mg/kg i.v. 1–2 times per week	Nausea, headache, rash, abdominal pain, vomiting, and diarrhea	Secondary prophylaxis

Note: Primary prophylaxis precedes any evidence of disease. Secondary prophylaxis prevents recurrence.

3. HIV-associated thrush or unexplained fevers >100 degrees for greater than 2 weeks

Cytomegalovirus (CMV) Retinitis

CMV retinitis is a vision-threatening illness that may affect up to 15% to 25% of AIDS patients. In immunosuppressed individuals, CMV can also cause a variety of other infectious complications including esophagitis, enteritis, colitis, hepatitis, encephalitis, transverse myelitis, and radiculitis. The management of CMV retinitis begins with a vigilant effort by the physician and patient to monitor for any persistent visual disturbance. AIDS patients with less than 50 to 100 CD4 cells should have an examination by an HIV-experienced ophthalmologist every 6 months and with any visual change (Table 29.3).

Cryptococcal Meningitis

Caused by the fungus *Cryptococcus neoformans*, this meningitis represents a significant hazard for patients with less than 50 CD4 cells and is the fourth most common cause of serious opportunistic infections. It often presents with nonspecific symptoms of fever, headache, malaise, and nausea. Stiff neck may or may not be present. Lumbar puncture and the finding of organisms by India ink or similar stain, or a positive cryptococcal antigen provides the definitive diagnosis. In patients with headache and fever, serum cryptococcal antigen provides an excellent screen for meningeal disease with 95% sensitivity (Table 29.3).

Mycobacterium Avium Complex Prophylaxis

Mycobacterium avium complex (MAC) causes disease in 15% to 40% of patients with HIV infection with symptoms including fever, night sweats, weight loss, abdominal pain, fatigue, diarrhea, anemia, and increased alkaline phosphatase (Table 29.3).

AIDS-Related Neoplasms: Kaposi's Sarcoma and B-Cell Lymphoma

Kaposi's sarcoma (KS) is an unusual neoplasm that seldom results in the death of the patient but contributes significantly to physical and psychological morbidity. It is seen much more often in homosexual men. Recent studies suggest that it may be initiated by a

herpes-family virus currently named Kaposi's Sarcoma Herpes Virus (KSHV). KS usually presents on the skin and often resembles a painless, fixed ecchymosis that becomes palpable. Lesions tend to range in size from 0.5 to 3 cm, and are usually purplish on light-skinned individuals and brown to black on those with darker skin. Because this is an overt sign of AIDS and many of those affected have seen friends with disfiguring facial lesions, the appearance of KS anywhere may have devastating emotional consequences. The course of KS is unpredictable. Even within the same individual quiescent periods may be followed by rapid dissemination of lesions. Spread is not confined to the skin, and gastrointestinal and pulmonary mucosal invasion is common. The diagnosis is easily made by punch biopsy, but the pathologist should be alerted to the possibility of KS. Treatment does not improve survival time and is therefore limited to symptom control of painful, bulky, disfiguring or obstructive lesions. Local radiotherapy is most frequently used, but intralesional vinbasatine or cryotherapy to facial lesions can be helpful. Systemic therapy with a variety of chemotherapeutic agents or alpha interferon has met with limited success. Table 29.3 describes treatment of opportunistic infections.

Antiretroviral Therapy for HIV Infection

Currently, there are three main classes of antiretroviral medication: nucleoside analogues, nonnucleoside analogues, and protease inhibitors. The approved nucleoside analogues include zidovudine (AZT), didanosine (ddI), zalcitabine (ddC), stavudine (d4T), and lamivudine (3TC). The protease inhibitors include saquinavir (Invirase), Ritonavir (Norvir), and Indinavir (Crixivan). The nonnucleoside analogues are currently undergoing clinical trials. Examples include nevirapine and delavirdine. Table 29.6 gives criteria for initiating antiretroviral therapy.

Guidelines for Using Antiretroviral Therapy

Consider treating HIV like TB or cancer. Use combination therapy, do not add drugs sequentially (increased chance of resistance) and change at least 2 drugs at once when making changes.
Do not use monotherapy (especially protease inhibitors).
Don't add a protease inhibitor to a failing regimen (same as using monotherapy because the virus is likely resistant to the current agents).

Table 29.6.
When to initiate antiretroviral therapy.

Considerations for Initiation of Antiretroviral Therapy

1. CD4 count less than 500/mm³ (or CD4% <25)-may defer if counts are stable for 18–36 months)
 2. Symptomatic HIV disease^a
 3. Rapid sustained fall in CD4 count
 4. Viral load >5,000–10,000 copies/mL (if CD4 is greater than 500/mm³, there are not data to support treatment)
-

^aSymptomatic disease includes symptoms such as recurrent mucosal candidiasis, oral hairy leukoplakia (OHL), chronic and unexplained fever, night sweats, and weight loss.

Generally two agents should be changed at once (add two agents, change one and add one).

Use full-dose therapy (after initial upward taper to avoid side effects) to prevent resistance.

Emphasize compliance.

Think about drug interactions (more of a concern with the protease inhibitors).

Monitor viral load (see above).

Think ahead about what you can change to when resistance develops.

Choice of Initial Antiretroviral Therapy

It is not clear if therapy in asymptomatic patients should be the most potent regimen (2 nucleosides and a protease inhibitor) or if this combination should be reserved for patients at greater risk of progression. (For a key to the following abbreviations, see the following table.)

Indications for Changing Therapy

A. Treatment failure

1. Increase in viral load or return toward pretreatment levels. Viral load should be measured before changing therapy and 3 to 4 weeks after initiating or changing therapy. The minimum reduction in viral load indicative of antiretroviral activity is 0.5-log (three-fold reduction).
2. Return of CD4 cell count to pretreatment levels.
3. Clinical disease progression.

AZT + ddI	→	→	→	→	AZT/3TC ± PI d4T/PI
AZT + 3TC	→	→	→	→	ddI/PI d4T/PI ddI/d4T d4T/3TC
AZT + ddC	→	→	→	→	AZT/3TC ± PI d4T/PI ddI/PI - only if patient is antiretroviral naive
ddI + d4T	→	→	→	→	AZT/3TC ddI/3TC/PI d4T/3TC/PI - caution of neurotoxicity
ddl (patients intolerant of combination therapy)	→	→	→	→	AZT/3TC ± PI AZT/ddI/PI d4T/PI

Figure 29.5. Suggested combinations for initial antiretroviral therapy for patients at lower risk of progression and choices for corresponding sequential combinations.

AZT/3TC/IDV	→	→	→	ddI/PI d4T/PI ddI/d4T
AZT/3TC/RIT	→	→	→	ddI/PI d4T/3TC/PI ddI/3TC/PI
ddI/d4T	→	→	→	AZT/3TC/PI d4T/3TC/PI ddI/3TC/PI
AZT/ddL/NVP (patients with CD4 cells 200-600/mm ³)	→	→	→	AZT/3TC/PI ddI/3TC/PI d4T/3TC/PI
AZT or ddI or d4T ± 3TC + protease inhibitor	→	→		AZT/3TC ± PI AZT/ddL/PI d4T/PI

Figure 29.6. Initial combinations and corresponding recommended sequential combinations of antiretroviral agents for patients at high risk of progression.

Table 29.7.
Antiretroviral medications.

Medication	Adult Dose	Monitoring	Side Effects	Cost
Zidovudine (AZT)	200 mg tid	CBC every 2–4 weeks for 3 months, then every 3 months	Anemia-Hb <8.0 (1.8%), neutropenia-ANC <750 (5.4%), headache (27%), fatigue (23%), nausea (29%), myalgia (6%)	~\$3000 per year
Didanosine (ddI)	125 mg bid if <60 kg 200 mg bid if >60 kg	Intermittent CBC and LFTs	Acute pancreatitis (5–9%), painful peripheral neuropathy (5–12%), nausea/vomiting, hepatic failure	~\$2000 per year
Zalcitabine (ddC)	0.375 mg q 8 h if <45 kg 0.75 mg q 8 h if >45 kg	Intermittent CBC and LFTs	Peripheral neuropathy (17–31%), rash, stomatitis, esophageal irritation, pancreatitis (1%)	~\$2300 per year
Stavudine (d4T)	30 mg q 12 h if <60 kg, 40 mg q 12 h if >60 kg	Intermittent creatinine and LFTs	Peripheral neuropathy, elevated liver enzymes	~\$2000 per year
Lamivudine (3TC)	150 mg bid	CBC every 2–4 weeks for 3 months, then every 3 months	3TC plus AZT: Anemia-Hb <8.0 (2.9%), neutropenia-ANC <750 (7.2%), headache (35%), fatigue (27%), nausea (33%), myalgia (8%)	~\$2500 per year

Table 29.7 (continued).
Antiretroviral medications.

Medication	Adult Dose	Monitoring	Side Effects	Cost
Nevirapine (Viramune)	200 mg qd x 14 d. then 200 mg bid	Intermittent LFTs	Rash (17%), increased GGT >450 U/L (2.4%)	
Saquinavir (Invirase)	600 mg tid	Same as for AZT	Diarrhea (3–4%), abdominal discomfort (2–4%), nausea (2–3%)	~\$7000 per year
Ritonavir (Norvir)	600 mg bid	Intermittent LFTs	Monotherapy: Nausea (23–26%), abdominal pain (3–7%), vomiting (13–15%), circumoral paresthesias (3–6%), increased LFTs, increased cholesterol	~\$7000 per year
Indinavir (Crixivan)	800 mg q 8 h	Intermittent LFTs	Monotherapy: Nausea (12%), vomiting (4%), increased bilirubin (8%), abdominal pain (9%), nephrolithiasis (3%)	~\$7000 per year

- Saquinavir, Ritonavir, and Indinavir represent protease inhibitors.
- Nevirapine is a nonnucleoside reverse transcriptase inhibitor.

- B. Toxicity, intolerance, or noncompliance.
- C. Current use of suboptimal treatment regimen.

Figure 29.5 lays out combinations of an initial antiretroviral therapy for patients at lower risk of progression, while Figure 29.6 suggests combinations for initial retroviral therapy for patients at high risk of progression. Table 29.7 details antiretroviral medications.

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Less Common Infectious Diseases in Primary Care

Richard I. Haddy

LEGIONNAIRES' DISEASE

Description of Pathogen and Epidemiology

The causative organism of legionnaires' disease is *Legionella pneumophila*, which is from the Legionnellaceae family. *L. pneumophila* is thought to cause about 90% of infections caused by bacteria in the Legionnellaceae family. *L. pneumophila* contains 14 serogroups, but serogroups 1, 4, and 6 are thought to cause the bulk of human infections. *L. pneumophila* is a Gram-negative, aerobic, nonspore-forming rod. The natural habitat for *L. pneumophila* appears to be any natural or manmade body of water. The organism proliferates in cooling towers and water distribution systems, which provide a favorable environment, and is also found in hot water tanks. It is thought that contaminated aerosols may disseminate the organism to humans from airstream exits of cooling towers or evaporative condensers. It is felt, however, that the primary reservoir for dissemination for the organism is water distribution systems.

While some research has ranked *L. pneumophila* among the most common etiologies of community-acquired pneumonia, it is felt that only a small percentage of cases of legionnaires' disease is correctly diagnosed. Major risk factors for the disease include cigarette smoking, chronic obstructive pulmonary disease, advanced age, and immunosuppression. Nosocomial *L. pneu-*

mophila cases are occasionally reported in children. This is most common in neonates, children who are immunosuppressed, and in children with chronic pulmonary disease. *L. pneumophila* infection is also seen in acquired immunodeficiency syndrome (AIDS).

Clinical features

Pneumonia is the major clinical finding in legionnaires' disease. Legionnaires' disease should be differentiated from Pontiac fever, which, while caused by *L. pneumophila*, is an acute, self-limiting, febrile illness without pneumonia.

The incubation period for legionnaires' disease is from 2 to 10 days. Early in the illness the patients usually have fever, anorexia, myalgia, and headache. The cough is initially mild. Interestingly, watery diarrhea is seen in 25% to 50% of the cases. Headache is often quite prominent. Physical examination may reveal localized rales and classical signs of pulmonary consolidation. Hyponatremia is more common in legionnaires' disease than in other kinds of pneumonias. Chest radiographs are positive, and the initial infiltrate is often alveolar and unilateral with lower lobe predominance. The disease is frequently missed because it is difficult to differentiate clinically from other forms of pneumonia. Clues that would make the physician think about legionnaires' disease may be a Gram stain of sputum with a predominance of neutrophils over bacteria, hyponatremia, occurrence in an environment where the water is known or suspected to be contaminated with *L. pneumophila* or failure of pneumonia to respond to beta-lactam antibiotics.

L. pneumophila disease outside of the pulmonary system has been documented in immunosuppressed patients. These disease entities would include perirectal abscess, sinusitis, cellulitis, pericarditis, endocarditis, and pyelonephritis.

Laboratory Diagnosis

The definitive method for diagnosis of legionnaires' disease is isolation of the organism from the sputum on buffered charcoal yeast extract agar (BCYE) supplemented with polymyxin, anisomycin, vancomycin, and dyes. However, the diagnosis of legionnaires' disease may be more commonly made by indirect fluorescent antibody in enzyme-linked immunosorbent assay. Acute and convales-

cent sera are drawn at a 4- to 12-week interval, and diagnosis is based on a four-fold rise of antibody titers to 1:128. If the prevalence of *L. pneumophila* antibody titers within the community is known to be low, a single elevated indirect fluorescent antibody titer of 1:128 may be diagnostic.

Treatment

A macrolide antibiotic combined with rifampin is a recommended initial treatment for acute cases of legionnaires' disease. Erythromycin is probably still the macrolide of choice, though azithromycin, clarithromycin, and roxithromycin are also felt to be highly effective against the organism. Ciprofloxacin and pefloxacin are the most common quinolone antibiotics used. If erythromycin is used, the recommended dosage is 2 gm orally or 4 gm intravenously per day. The duration of antibiotic therapy is from 10 to 14 days, though longer duration of antibiotic therapy is generally recommended for immunosuppressed patients. Other antibiotics that are effective against the organism are trimethoprim-sulfamethoxazole and the tetracyclines. A macrolide antibiotic is recommended for immunocompetent patients with community-acquired pneumonia.

The mortality rate for legionnaires' disease is quite low in immunocompetent patients, although the mortality may approach 50% in nosocomial infections.

LYME DISEASE

Description of Pathogen and Epidemiology

The disease is caused by the tick-transmitted spirochete *Borrelia burgdorferi*. The vectors of the disease are the ticks *Ixodes dammini* in the northeastern and midwestern United States and *I. pacificus* in the West. *I. dammini* larva and nymphs generally feed on rodents, usually white-footed mice, and adults generally feed on larger animals, mainly deer, which are abundant in endemic areas of New England. Human disease occurs when humans intervene in the ecology of these ticks, *B. burgdorferi*, rodents, and larger mammals. It is thought that ticks must be attached to the skin for at least 24 hours for transmission of the organism to occur. While Lyme disease occurs in other countries, in the United States it occurs mainly in three areas: the Northeast, Wisconsin and Minnesota of the Midwest, and in California and

Oregon. Most illness occurs between May and November with peak onsets in midsummer.

Clinical Features

Lyme disease is difficult to diagnose and is probably over diagnosed. The most difficult problem is distinguishing features of this disease from chronic fatigue syndrome, fibromyalgia, chronic pain syndromes, anxiety, depression, or other states of psychological stress. Similar to syphilis, Lyme disease is thought to occur in three stages. Stage 1 consists of localized erythema chronicum migrans (ECM), stage 2 is disseminated infection, and stage 3 is persistent, chronic infection.

ECM begins as a red macule or papule at the site of the tick bite. The area of redness expands around the center with partial clearing in the center. The full lesion averages 15 cm in diameter. The thigh, axilla, and groin are common sites for the lesion, although the lesion can be located virtually anywhere on the body. About 50% of the patients develop other annular secondary lesions within several days of onset of the initial skin lesion. Some patients develop a nonspecific macular rash along with these lesions, and ECM usually fades within 3 to 4 weeks. ECM is generally accompanied by regional lymphadenopathy and flulike symptoms such as headache, myalgias, fatigue, fever, and chills.

Within a few weeks to months of onset of the disease, most patients have joint symptoms ranging from migratory joint pain to frank arthritic swelling and erosive synovitis. Eventually, the patient may have attacks of arthritis, separated by complete remissions, which last from a few weeks to months.

Symptoms of meningeal irritation may occur early in the illness when ECM is present. After several weeks to several months, the common pattern is of symptoms of meningitis, headache, with superimposed facial palsy or peripheral radiculopathies. In patients with meningitis, the cerebrospinal fluid rarely has more than 100 cells/mm, most of which are lymphocytes. Stage 3, if it occurs, begins usually years after the onset of the disease but sometimes months after. The patient may develop a chronic encephalopathy, which may affect mood, memory, or sleep.

A small percentage of patients with Lyme disease have cardiac involvement within the first several weeks of the illness. The

most common manifestation is varying degrees of atrioventricular block. This would include first-degree atrioventricular block, Wenckebach phenomenon, or complete heart block. The period of heart involvement is usually brief (a matter of days), and insertion of a permanent pacemaker is considered unnecessary. The diagnosis of Lyme disease should be considered in an otherwise healthy patient in a Lyme disease endemic area who develops atrioventricular heart block.

Laboratory Diagnosis

While the organism may be cultured from the edge of an erythema migrans lesion, diagnosis is usually made by serological testing. Serological testing early in the infection is not sensitive because the immune response in this disease develops slowly. However, later in the illness serological testing can be performed with a high degree of sensitivity and specificity. Perhaps the most commonly used serological test is the enzyme-linked immunosorbent assay (ELISA). Other serological tests that are used are the indirect immunofluorescence assay (IFA), western blot testing, and antibody-capture immunoassay (EIA). Most other laboratory abnormalities in the disease are nonspecific.

Treatment

Most stages of manifestations of Lyme disease can be treated with oral antibiotic therapy. Early in the illness doxycycline 100 mg twice daily or amoxicillin 500 mg three times daily for 10 days is probably adequate. Other antibiotics that are considered effective against the organism are cefuroxime axetil and erythromycin. In patients with disseminated infection, 20 to 30 days of oral antibiotic therapy is recommended.

In patients with a neurologic involvement, intravenous antibiotic therapy is considered necessary. Ceftriaxone, 2 gm per day for 3 to 4 weeks is commonly used, but cefotaxime (2 gm every 8 hours) or penicillin G (5 million units every 6 hours) is also considered effective.

A more difficult problem is whether patients with tick bites should receive prophylactic antibiotic therapy. In general, if the patient is very anxious about contracting the disease, if the tick is seen to be engorged with blood, or if a follow-up with the patient

is potentially difficult, the physician may elect to treat with a 10-day course of amoxicillin or doxycycline.

ROCKY MOUNTAIN SPOTTED FEVER

Description of Pathogen and Epidemiology

Rocky Mountain spotted fever (RMSF) is a member of the "spotted fevers" group of illnesses caused by closely related rickettsiae transmitted by ticks and mites. The spotted fevers are in turn part of a larger group of rickettsial infections.

The etiological agent, *Rickettsia rickettsii*, is an obligatory intracellular Gram-negative bacterium. It is transmitted in the eastern states by the American dog tick, *Dermacentor variabilis*, which is both the vector and the main reservoir. It is transmitted by the Rocky Mountain wood tick, *D. andersoni*, in the western states. Only adult *Dermacentor* ticks feed on humans, but the disease may also be transmitted when the tick is removed and possibly crushed between the fingers when one may be exposed to infective tick hemolymph.

While at one time the disease was thought to exist only in the Rocky Mountain states, at present the disease incidence is higher in the South Atlantic states and the West South Central states. The disease is most commonly seen during the late spring and summer.

Clinical Features

Diagnosis of Rocky Mountain spotted fever is generally based on clinical manifestations. Early diagnosis may be difficult but is important because of the relatively high mortality associated with the disease if not treated in a timely fashion. In RMSF the early manifestations of the disease are fatigue, myalgias, spiking fever, and headache, which is usually quite severe. Gastrointestinal involvement may be marked and may include abdominal pain, nausea, vomiting, or diarrhea. The rash appears 3 to 5 days after the onset of fever. It usually starts on the ankles and feet and moves to the wrists and hands and then to the trunk and head. The rash starts out red, macular, and blanches to pressure. It may become papular and darker red and is usually edematous. Within 2 to 3 days it may become petechial and purpuric. Ten percent or more of patients with the disease may not have a rash (Rocky Mountain "spotless" fever), and this happens more often in older or

African-American patients. In a small number of patients, the rash may progress to skin necrosis or gangrene of the digits or limbs, occasionally requiring amputation. Meningismus, focal neurologic deficits, or transient deafness may ensue, and neurologic involvement may indicate a poor prognosis. Renal failure may ensue in severe RMSF. Pulmonary involvement may be manifested by cough, pulmonary infiltrates on chest x-rays, pleural effusion, or frank pulmonary edema. Hyponatremia is observed in more than half of the patients.

The disease is easily confused with measles in unimmunized patients. In RMSF, however, the rash is more edematous, and often starts on the face with measles, while it almost never does in RMSF. The rhinorrhea, cough, and conjunctivitis that are typical of measles are unusual in RMSF. The rash of meningococcemia is frequently confused with RMSF. The rashes of both diseases may be petechial at one point, but the rash of meningococcemia usually becomes purulent and necrotic quite early. Most patients with meningococcemia also have meningitis, and meningeal signs are often marked.

Laboratory Diagnosis

The diagnosis of RMSF is largely clinical, since serology, the usual method for confirmation of the diagnosis, is retrospective. Acute and convalescent serum should be drawn on patients suspected of RMSF. Indirect hemagglutination and indirect immunofluorescence are the most sensitive and specific serological tests for RMSF, and the diagnostic titers are 1:28 for indirect hemagglutination and 1:64 for indirect immunofluorescence and latex agglutination.

Treatment

RMSF is treated with oral tetracycline 25 to 50 mg/kg/day or chloramphenicol 50 to 75 mg/kg/day given in 4 divided doses for 7 days. Doxycycline 100 mg every 12 hours for 7 days is also quite effective. The drugs should generally be continued for 2 days after the patient has been febrile. Tetracycline or chlorphenicol should be given intravenously in patients with marked nausea and vomiting or if otherwise severely ill. The organism is also susceptible to rifampin and ciprofloxacin and pefloxacin. Fluid and electrolyte maintenance is often important in this illness because of increased vascular permeability. Without treatment, death may occur within 8

to 15 days in 20% of patients. The disease is considered more lethal in the elderly and in men.

Preventive measures include use of protective clothing and regular checks of the entire body to carefully and completely remove ticks with forceps to prevent rickettsial transmission.

TUBERCULOSIS

Description of Pathogen and Epidemiology

Tuberculosis is caused by *Mycobacterium tuberculosis* and, less commonly, *M. bovis*, both of the family *Mycobacteriaceae*. *M. tuberculosis* is an aerobic, nonspore-forming, nonmotile bacillus. It is an acid-fast bacillus, meaning that certain water-soluble dyes that are taken up through the wall of the bacillus cannot be eliminated by an acid wash. The organism is usually cultured by the BACTEC radiometric system. Mycobacterial growth is slow, and colonial growth usually takes 4 to 6 weeks.

Transmission is generally by inhalation of infectious droplets aerosolized by coughing, talking, or sneezing. Two important factors in the spread of this disease are crowded living conditions and a population with little inherent resistance to the organism. Tuberculosis is now most common in medically underserved populations, urban indigents, the homeless, migrant farm workers, alcoholics, intravenous drug users, and in prisons. Active tuberculosis is now most commonly found in young adults because this is the population with the highest prevalence of HIV infection. AIDS may be the strongest risk factor currently for tuberculosis. The periods in life in which the infection is most common are infancy, early adulthood, and old age.

Clinical Features

Tuberculosis is generally a pulmonary disease, but virtually any site in the body can be involved, and this would include miliary tuberculosis, central nervous system tuberculosis (specifically tuberculous meningitis), tuberculous pleurisy, tuberculous pericarditis, skeletal tuberculosis (including Pott's disease), genitourinary tuberculosis (including renal and genital tuberculosis), gastrointestinal tuberculosis, tuberculous peritonitis, tuberculous lymphadenitis (scrofula), and other sites. Early pulmonary tuberculosis is asymptomatic and usually found incidentally on chest x-ray. As the disease progresses, however, systemic symptoms such as fatigue,

anorexia, weight loss, chills, afternoon fever, and night sweats ensue. A productive cough is present with mucopurulent sputum. Hemoptysis occurs in advanced disease. Physical findings are nonspecific or absent. Post-tussive rales may be heard as well as whispered pectoriloquy or tubular breath sounds. Classic findings in adults on chest x-ray include patchy infiltrates in the apical areas of the upper lobes or the superior segment of the lower lobes. Cavity formation would further arouse suspicion. In children the initial focus is more commonly in the midlung zones.

Diagnosis

Virtually all patients demonstrating 15 mm or more of skin induration to an intracutaneous injection of 5 tuberculin units (TU) of purified protein derivative (PPD) should be considered infected with *M. tuberculosis*. False positive reactions are virtually all due to infection with nontuberculous mycobacteria, and false negatives may be caused by reticuloendothelial disease, therapy with corticosteroids, and intercurrent viral infections. Induration of 5 mm or more in people with HIV infection should be considered positive and sufficient to warrant chemoprophylaxis. A negative tuberculin reaction is common and may be expected in AIDS patients with tuberculous infection.

Diagnosis in pulmonary tuberculosis may be made with three daily morning sputum specimens for acid-fast stain and culture. When sputum is not produced, morning aspiration of gastric contents is a classical method of diagnosis. Diagnosis may also be made with transbronchial biopsy and bronchial washings from fiberoptic bronchoscopy. Culture of three morning urine specimens on separate days usually suffices for diagnosis in renal tuberculosis. Tuberculosis may present atypically in the elderly, mimicking other forms of bacterial pneumonia.

Chemoprophylaxis

Chemoprophylaxis is recommended in patients less than 35 years of age who have ≥ 15 mm induration on 5TU PPD and who have no risk factors and are in a low-incidence group. This would consist of isoniazid therapy 300 mg daily given orally for 6 months. Twelve months of isoniazid (INH) therapy are recommended in HIV-infected patients. Patients less than 35 years of age with ≥ 10 mm induration on 5TU PPD in a high-incidence group with no

risk factors are also recommended for standard chemoprophylaxis. Initial and periodic monitoring of liver function tests is recommended in patients 35 years of age or older receiving INH and in patients with a history of alcoholism, liver disease, or intravenous drug use. Pyridoxine supplementation, 10 to 25 mg daily, is recommended in patients being treated with diabetes, alcoholism, chronic renal failure, pregnancy, malnutrition, patients being treated with anticonvulsants, and in elderly patients. Chemoprophylaxis is recommended in most tuberculin-positive contacts of active cases who are less than 50 years of age.

Treatment of Tuberculosis

Almost all forms of drug-sensitive tuberculosis both pulmonary and extrapulmonary will be responsive to the standard 9-month regimen of INH (300 mg daily) plus rifampin (RMP) (600 mg daily) by mouth. Some authorities advise the addition of pyrazinamide (PZA) (25 to 35 mg/kg daily) plus either streptomycin (STM) (1 g) or ethambutol (EMB) (25 mg/kg) initially until sensitivity results are available, especially in geographic areas where drug resistance is a possibility. Six-month treatment regimens are also available. One acceptable 6-month regimen is 2 months of INH, RMP, and PZA (plus either EMB or STM if INH resistance is suspected) followed by INH and RMP daily for 4 additional months. Early morning sputum cultures should be obtained at least monthly after initiation of therapy to monitor conversion of sputum cultures to negative. Sputum cultures should convert to negative within 2 months and, if they do not, drug resistance should be suspected. Pulmonary tuberculosis in children is treated with INH (10mg/kg daily) and RMP (15mg/kg daily) for 1 year.

Patients with AIDS or other immune-deficient status, who exhibit skin test conversion, may be treated for 6 months with regimens normally reserved for active tuberculosis. Drug regimens for treating AIDS patients infected with active tuberculous disease do not differ from those in non-AIDS patients except treatment should be continued for a total of 9 months or at least 6 months beyond sputum culture conversion to negative.

A patient may have a positive tuberculin test administered within days to a year of a negative one due to restimulation of remotely established hypersensitivity (the booster effect). This should be kept in mind when two tuberculin tests are adminis-

tered near each other in time and should be taken not to overinterpret the second test (i.e., to infer conversion).

Suggested Readings

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Endocrinology in Primary Care

Chapter 31

Diabetes Mellitus

Manuel Tzagournis and David R. Rudy

PATHOPHYSIOLOGY

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia. A deficiency of insulin or a resistance to its action is responsible for the abnormalities. Diabetes is a common disorder that occurs worldwide, but is especially prevalent in developed countries that have ample food for their citizens.

Insulin controls glucose uptake by cells and fuel conservation and expenditure. Glucose and other substrates stimulate its secretion from islet cells of the pancreas. Minor elevations of glucose levels in the blood cause the release of insulin that reaches peak values within 30 minutes to 1 hour. A return to basal concentration occurs 2 or 3 hours after the meal. During this time, insulin enhances the uptake of glucose by most tissues that use it for energy. Simultaneously, insulin carries out its other major function; namely, storing calories for use when exogenous nutrients are not available. Insulin converts glucose to glycogen, stimulates the uptake of amino acids to be stored as protein, and permits glu-

cose metabolic products to be synthesized into triglycerides while inhibiting lipolysis from fat. During the fasting state opposite changes occur. Glucose levels diminish resulting in low insulin levels in the blood. Thus, glucose is not taken up by most cells, although the brain continues to require glucose for energy. Low levels of insulin signal the release of fatty acids, which provide most of the energy needs of the body. Glycogen can readily furnish glucose for "urgent" needs, and protein breaks down to specific certain amino acids for new glucose formation (gluconeogenesis).

One can understand the principle aspects of diabetes mellitus by comparing it to an exaggerated fasting state. Abnormally low insulin causes reduced glucose uptake, while new glucose formation, stimulated by amino acids and free fatty acids, accelerates in the liver. As glucose levels increase and exceed the renal threshold for reabsorption, calories, electrolytes, and water are lost in the urine. Free fatty acids released in excess from fat cells are partially oxidized to ketones and acetoacetic acid resulting in acidosis.

Because diabetes influences so many metabolic processes and is associated with specific complications, the economic impact of the disease is enormous. More than 10 million Americans have diabetes, and almost half are undiagnosed. It is the most common endocrine disease that clinicians treat.

Types of Diabetes Mellitus

There are two important, time-honored classifications of diabetes mellitus. Type I (insulin-dependent diabetes mellitus) and type II (noninsulin-dependent diabetes mellitus) make up the predominant forms throughout the world. Less common types are recognized and include those associated with pancreatic disease, certain drugs, endocrine disorders, and rather rare genetic conditions. Table 31.1 outlines a practical classification of diabetes. Present classifications have shortcomings because of overlap and heterogeneity of type II diabetes.

Type I - Insulin-Dependent Diabetes Mellitus (IDDM)

These patients have a deficiency of insulin and are ketoacidosis prone. Exogenous insulin is required to prevent ketoacidosis and sustain life. The rapidity of onset varies so that some type I patients resemble noninsulin-dependent patients for months to

Table 31.1.
Classifications of diabetes mellitus.

-
- I. Type I (Insulin-dependent diabetes)
 - II. Type II (Noninsulin-dependent diabetes)
 - A. Nonobese
 - B. Obese
 - III. Other types
 - A. Pancreatic disease
 - B. Endocrine disorders
 - C. Drug-induced
 - D. Genetic syndromes
 - IV. Gestational diabetes
 - V. Impaired glucose tolerance
-

years. More than 1 million individuals in the United States have IDDM, although considerably more take insulin in order to better control hyperglycemia.

The pathogenesis of type I diabetes involves genetic susceptibility, environmental injury, and an autoimmune reaction that involves and eventually destroys the beta cells of the pancreas.

There is a strong association between type I diabetes and the human leukocyte antigens (HLA) on the chromosome containing the major histocompatibility region. The presence of HLA-DR3 or HLA-DR4 alone or together is found in approximately 90% or more of Caucasians with type I diabetes. Interestingly, certain HLA types afford protection against type I diabetes. The exact genetic inheritance is not known. Less than half of identical twins of type I diabetics concordantly develop the disease (1). It is postulated that a virus or other stimulus triggers events that produce immune responses in predisposed people. Antibodies directed against the islet cell can be detected in a high proportion of individuals diagnosed with type I diabetes, but detectable antibody levels tend to decrease with duration of disease. Thus, a genetically prone individual may have the misfortune to develop a viral infection (e.g., Coxsackievirus B4) or a sensitivity to a protein (e.g., bovine albumin) that stimulates antibodies and an autoimmune reaction. Insulinitis can ensue with destruction of pancreatic beta cells, and the development of clinical diabetes mellitus. Table 31.2 summarizes major features of type I and type II diabetes.

Table 31.2.**Characteristics of type I compared with type II diabetes.**

	Type I	Type II
Age of onset	Young	Older (>40)
Body weight	Normal or thin	Obese
Onset of symptoms	Usually rapid	Usually slow
Ketoacidosis	Common	Uncommon
HLA association	Present	Absent
Islet cell antibodies	Present	Absent
Insulinitis	Yes	No
Insulin resistance	Usually absent	Usually present

Type II - Noninsulin-Dependent Diabetes (NIDDM)

Patients with type II diabetes can be found in all age groups, but prevalence increases with age. About 80% of individuals are overweight at the time of diagnosis. Insulin resistance is the characteristic finding rather than insulin deficiency, although fasting hyperglycemia is associated with a deficiency of insulin (2). Onset of symptoms is gradual, and some patients can be asymptomatic for years. It is a heterogeneous disorder, and several molecular biologic disturbances have been identified in the form of abnormal receptors or cellular glucose transporting proteins.

The prevalence of NIDDM is estimated to be about 5% of the adult population. A population between 70 and 79 years of age has a several-fold increase in the frequency of diabetes compared with the 40- to 49-year age group (3).

In contrast to type I diabetics, there is a much lower association with HLA, insulin antibodies, or insulinitis in type II patients. There is overlap in the two types. An older person can have a quite typical presentation of type II diabetes, but years later found to need insulin and have autoimmune destruction of islet cells typical of type I diabetes. Familial inheritance of type II diabetes is strong, probably multifactorial, but poorly understood. Certain factors such as overeating, obesity, inactivity, extraordinary stress, endocrine disorders, or medications increase the risk of clinical expression of diabetes.

Insulin concentrations may be high, normal, or deficient (4). Insulin resistance is common, and as long as the islet cells are able to respond adequately, elevated insulin levels are found. Insulin

resistance leads to hyperinsulinemia, in most type II diabetes. Hyperinsulinemia carries unfavorable effects on lipids, is an important contributing cause of the hypertension so often present in type II diabetes and their families and is an independent risk factor for ischemic heart disease (4). High insulin or C-peptide concentrations in people with normal glucose tolerance have been associated with increased risk of developing type II diabetes (2). Pima Indians and Hispanics tend to have high insulin levels, insulin resistance, and increased prevalence of diabetes, especially with obesity. Insulin secretion also tends to be abnormal. There is lack of a brisk early response to increasing glucose levels that is present in nondiabetic people. The biological activity of insulin in type II diabetics seems to be normal. Patients' insulin can resume its effectiveness to varying degrees in obese type II diabetes if the patients succeed in losing weight. As hyperglycemia becomes more severe, insulin secretion diminishes and can resemble that of a type I diabetic. Clinically, this is noted when fasting glucose levels are consistently above 160 mg/dL (5).

Some type II diabetics can revert to normal biochemical and hormonal profiles by eliminating known risk factors. Loss of weight, increase in activity or conditioning, and elimination of aggravating influences (e.g., thiazides or steroids) are examples of such factors.

Other Types of Diabetes Mellitus

Occasionally, individuals have hyperglycemia secondary to other conditions, drugs, or genetic disorders. The diabetes may be temporary, such as a gestational period of pregnancy. Impaired glucose tolerance implies an inability to achieve normal glucose values after glucose ingestion, but criteria of definite diabetes are not met.

The pancreas can be damaged by inflammation, tumor, or hemochromatosis resulting in islet cell pathology and clinical diabetes. Endocrine disorders such as acromegaly, Cushing's syndrome, hyperaldosteronism and pheochromocytoma are associated with increased frequency of diabetes. Sometimes the diabetes disappears with successful treatment of the underlying condition. A number of drugs elevate glucose, the most common ones include corticosteroids and thiazide preparations. Included in "other types" of diabetes are those closely linked with genetic disorders. Some of the neuromuscular syndromes (Friedreich's

ataxia or acanthosis nigricans) with antibodies to insulin receptors are examples. Gestational diabetes may be the first manifestation of permanent diabetes, or the hyperglycemia may never appear again after the pregnancy has ended. Similarly, impaired glucose tolerance noted during periods of stress (emotional, malnutrition, or infections) may not recur. It is worthwhile to think about these "other" types of diabetes when diabetes is initially diagnosed so that the appropriate diagnostic tests can be obtained.

Clinical Manifestations

The symptoms and signs of type I and type II diabetes are similar. The degree of hyperglycemia, as well as its duration, is largely responsible for the clinical presentation of a particular patient. An individual may be totally asymptomatic with diabetes or severely ill in diabetic ketoacidosis and coma.

Polyuria, polydipsia, and polyphagia with weight loss are the classic symptoms reflecting moderate to severe hyperglycemia. The symptoms in older type II diabetes tend to be more subtle and insidious. Complaints of fatigue, blurred vision, or monilial infections, particularly vaginitis are common. Other symptoms include furuncles, skin infections, numbness or tingling of the feet reflecting early neuropathy, weakness, and general malaise. Unusual clinical presentations may occur that challenge the clinician, such as pain or weakness in the hand from carpal tunnel syndrome or a painful mass resulting from an infarction of muscle. Prior to the diagnosis of diabetes some patients have reactive hypoglycemia with complaints of hunger, sweating, palpitations, and tremor several hours after a meal that is rich in simple sugars. Such patients have a delayed insulin secretion with elevated levels following a meal.

Infection, stroke, or myocardial infarction can produce marked hyperglycemia as an initial manifestation of diabetes. Polyuria, dehydration, and a low blood pressure are not unusual in these patients. Deep prolonged respirations in a lethargic or comatose patient suggests ketoacidosis. The breath may have a fruity odor. Nausea, vomiting, or abdominal pain are common. The clinician must think about diabetes in patients with uncharacteristic clinical presentations. Diabetes has become the syphilis of several generations ago in the variety of ways that it affects people.

Diagnosis

The diagnosis of diabetes mellitus has been simplified in recent years. Rarely is it necessary to do a glucose tolerance test. A good history and physical examination prompts the physician to do appropriate testing to rule out underlying conditions that might be present, such as pancreatic disease or other endocrine disorders. However, most diagnostic efforts are directed to confirming the presence of hyperglycemia.

When at least two measurements of the fasting plasma glucose exceed 140 mg/dL in any age group, the diagnosis of diabetes is secure. In the presence of classic symptoms or signs a random plasma glucose level of 200 mg/dL or greater is also diagnostic. In borderline cases when the glucose values do not reach the criteria mentioned above, an oral glucose tolerance test can be ordered.

To properly interpret the glucose tolerance test the individual should eat normal amounts of carbohydrates the day or two before testing. Also, the individual should be free of an acute illness, and physically active. Following a fast of about 12 hours, a glucose solution containing 75 gm of glucose or 1.75 gm/kg for children is given orally. Glucose concentrations are determined at baseline, 30, 60, and 120 minutes after ingestion. If two values exceed the criteria outlined in Table 31.3, a diagnosis of diabetes can be confirmed, gestational diabetes not included.

The criteria for the diagnosis of gestational diabetes are slightly different from nonpregnant criteria and are addressed in the section on diabetes and pregnancy.

Table 31.3.

Criteria for the diagnosis of diabetes mellitus by the oral glucose tolerance test.^a

	Normal Values (plasma venous glucose mg per dL)	Diabetes Mellitus
Baseline	<115	140 or greater
30 or 60 minutes	<200	200 or greater
120 minutes	<140	200 or greater

^aIntermediate values between normal and diabetes mellitus indicate impaired glucose tolerance.

Treatment

Rather than detailed diabetic diets, the concept of proper nutrition should prevail as an indispensable part of the treatment of all diabetics. Likewise, physical activity is important in long-term management of any type of diabetes. Oral hypoglycemic agents are an option for type II diabetics who are not responsive to nutritional changes and exercise. Insulin is the ultimate hormonal replacement therapy for type I diabetics and for all other diabetics who require it for satisfactory control of hyperglycemia. Diabetes is a life-time disorder, and an extremely personal chronic disease. The more a patient knows, the better that person can cope with it. A good understanding of diabetes makes the patient a team member and rationalizes the need for home glucose monitoring. The tools of maintaining good control are now readily available with follow-up assessments using glycosylated hemoglobin measurements and self-testing of glucose at home. Although home glucose monitoring is inconvenient and painful, it has improved the ability to control hyperglycemia tremendously. Noninvasive methods to quantitate glucose without breaking the skin are actively being tested and improved.

An important study, the Diabetes Care and Complications Trial (DCCT), demonstrated impressively that tight glycemic control significantly reduced retinopathy, nephropathy, and neuropathy (6). The trial, however, resulted in an increase in hypoglycemic incidents. Although the participants were type I diabetics, many diabetologists feel that similar benefits would accrue to type II diabetics as well.

Nutritional Principles

A nutritionist or dietitian is a valuable member of the team. Some patients will adhere to an American Diabetes Association (ADA) diet with food exchanges, but others prefer to learn general guidelines of proper nutrition. The fundamental nutritional requirements are similar whether or not a person is diabetic. But proper timing of intake, amount of calories, and composition of food help a person with abnormal insulin dynamics to avoid the extremes of glycemic swings. The time of food ingestion and amount should reflect the habits and lifestyle of the insulin-requiring patient. Whenever possible, adjust the insulin dose, not necessarily the pattern of eating.

The number of calories, the composition of the diet, and its distribution throughout the day are the key features of the nutritional prescription. The patient should eat or drink rapidly absorbed sugars if hypoglycemia occurs, and semisolid food or liquids containing carbohydrate and electrolytes are recommended for sick-day management.

Calorie Estimation. Calories sufficient to maintain or achieve ideal body weight should be estimated. Since more than 80% of type II diabetics are overweight at the time of diagnosis, caloric restriction is common advice. A simple guideline for adults to estimate the desirable weight appears in Table 31.4. For example, a woman with an average frame who is 5 feet, 5 inches tall should weigh about 125 pounds. Multiplying the desirable weight by 10 provides an estimate of the basal (sedentary) caloric requirement per day. In the above example, the basal caloric requirement is 1250 calories. From 10% to 40% additional calories can be prescribed, depending on the degree of physical activity for that individual. For infants and children, the caloric requirement is about 1000 calories for the first year plus approximately 100 calories for each additional year. Obviously, adolescents will require additional calories during growth spurts, as will pregnant or lactating women.

Composition of Nutrients. For diabetics, this is quite similar to those for healthy individuals without diabetes. Approximately 55% of total calories should be carbohydrates, preferably complex, high-fiber carbohydrates. Examples include whole wheat breads, oat bran, cereals, pastas, whole fruits, beans, and vegetables. Protein makes up about 15% of total calories, but people with diabetic nephropathy may need to take less. Total fat should be approximately 30% of the dietary calories with less than 10% in saturated

Table 31.4.
A single guide to estimate desirable weight.

Male	Female
5 feet—106 pounds Add 6 pounds for each inch	5 feet—100 pounds Add 5 pounds for each inch
Add 10% for large frame and subtract 10% for small frame	

fats. Monounsaturated fat found in olive oil, canola oil, and nuts are increasingly recommended as advantageous forms of fat, especially for those with abnormal lipid profiles. ADA guidelines suggest cholesterol intake of 300 mg per day or less. Limiting foods with high saturated fats and cholesterol such as eggs, whole milk, red meats, cheeses, and butter in favor of poultry, fish, low fat milk, olive oil, and small portions of lean meat with visible fat removed is a reasonable approach to meet the recommendations. Americans, in general, ingest too little fiber. Glycemic control and serum lipids improve when fiber intake increases.

Distribution of Calories. Scheduled meals and feeding is helpful in controlling glucose and preventing hypoglycemia. Nondiabetic individuals have great flexibility in what or when they eat. Consistency in meal composition and timing is especially important if insulin is needed. The diabetic patient, generally, can better handle three small meals and snacks between meals and at bedtime. A dietitian can help a patient to adjust to a treatment regimen with minimal disruption in lifestyle and cultural preferences. The exchange lists that are readily available educate patients about equivalent portions and composition of foods. Sugar substitutes such as saccharin or aspartane are perfectly acceptable to use. Alcohol in moderation (1 bottle of beer, or a glass of wine, or 1.5 ounces of distilled spirits) is also acceptable providing one is aware of the calories and the precautions applicable to the population at large. Alcohol is considered a fat exchange, or in the case of beer, a fat and starch exchange for those using the exchange lists.

Exercise

The only physiologic stress that increases glucose uptake by cells without requiring additional insulin is exercise. Fever, pregnancy, emotional upset all tend to elevate glucose levels in diabetics. Almost everyone can participate in some type of physical activity, preferably of the aerobic type. Begin by advising a patient to walk, swim, jog, or dance regularly at a pace the person can tolerate. Then very gradual increments can be made weekly. The benefits include improved glucose control, weight loss, improved lipid profile, and a sense of well-being.

In type I diabetics exercise can result in increased glucose levels and mild ketosis if insulin is inadequate because of catecholamine secretion. More commonly, one must be cautious

about hypoglycemia. A small snack is preferable to major insulin adjustments for moderate exercise, but for prolonged activity it is prudent to decrease the insulin dose. A vigorous exercise program should only be started after a medical evaluation with stress tests if there is suspicion of cardiovascular disease. In virtually every community supervised exercise programs are available. Individualizing a regular program of physical activity is an integral part of diabetic management.

Oral Hypoglycemic Agents

If nutritional advice and an exercise program are not sufficient to control glucose in type II diabetics, oral drugs offer an alternative to exogenous insulin. Most type II diabetics should be able to achieve basal or fasting glucose levels below 150 mg/dL, and postprandial concentrations below 200 mg/dL. The glycosylated Hgb level should be within the upper limits of normal. Oral drugs are needed to achieve that degree of control in approximately one-third of type II diabetics. Another one-third require exogenous insulin supplementation.

Until recently, only the sulfonylureas were available in the United States. Now metformin (Glucophage), a biguanide, is available. Phenformin, another biguanide formerly used throughout the world, was withdrawn in many countries because of an increased risk of lactic acidosis. Acarbose is also available and acts to retard carbohydrate digestion after meals, resulting in a blunting of the rise in postprandial glucose. Table 31.5 outlines features of selected oral agents.

The *sulfonylureas* act by stimulating insulin secretion; thus they are only effective in the presence of functioning islet cells. They also have an action on insulin receptors resulting in increased glucose uptake. Occasionally, they are useful in combination with insulin to smooth out glucose fluctuations. The first-generation drugs tolbutamide, tolazamide, acetohexamide, and chlorpropamide are used less frequently than the second-generation glyburide or glipizide. The dosage is gradually increased until glucose control is achieved. Then attempt to decrease the dosage gradually while maintaining glycemic control. Secondary failure after a period of improved control occurs in approximately 10% of patients per year. Combination therapy with metformin is frequently successful if a single-drug regimen is inadequate. Hypoglycemia may occur particularly in the elderly. Chlorpropamide

Table 31.5.
Features of selected oral hypoglycemic drugs.

	Drug	Common Dose (mg)	Dose Range (mg)	Actions	Dose Frequency
Sulfonylureas	Glipizide (Glucotrol)	5 mg	2.5–40 mg	Stimulates insulin secretion and increases glucose uptake	q.d. or b.i.d.
	(Glucotrol XL)	5 mg	5–20 mg		q.d.
	Glyburide (Diabeta)	5 mg	1.25–20 mg		q.d.
	(Glynase)	3 mg	0.75–12 mg		q.d.
	Glimepiride (Amaryl)	2 mg	1–8 mg		q.d.
Biguanides	Metformin (Glucophage)	1000 mg	500–2550 mg	Decreases hepatic glucose output and increases glucose uptake, reduces insulin levels	b.i.d.
Alpha-glucosidase inhibitor	Acarbose (Precose)	150 mg	75–300 mg	Delays carbohydrate digestion	t.i.d.

and other first-generation sulfonylureas may produce an antidiuretic hormone effect and hyponatremia. Rarely, allergic reactions occur. One study raised concern about increased cardiovascular mortality with a sulfonylurea as well as Phenformin (7).

Metformin, now available in the United States, was prescribed for many years in other countries. It is taken with breakfast and dinner at doses of approximately 500 mg twice a day. It acts to decrease hepatic glucose output, enhance glucose uptake, and possibly delay glucose absorption from the intestine. Because it decreases insulin resistance, metformin may have its greatest usefulness in obese patients (8). Hypoglycemia does not occur unless it is used in combination with insulin or a sulfonylurea. Lactic acidosis, although less frequent than phenformin, can occur, so it should not be used in patients with renal impairment, alcohol abuse, cardiac or pulmonary disease likely to be associated with hypoxia, severe infections, or liver disease.

Acarbose is a new hypoglycemic agent that inhibits alpha-glucosidase in the small intestine. The absorption of glucose from the gut is delayed resulting in diminished postprandial glucose concentrations. It can be used in combination with a sulfonylurea, and must be administered with meals containing carbohydrate. Flatulence is a common side effect. Rarely serum transaminase elevation occurs, and the drug is contraindicated in patients with inflammatory bowel disease, colonic ulceration, or renal dysfunction. The patient may start with one-half of a 50 mg tablet, then increase to one tablet with each meal. Other drugs are being developed that act on glucose transporters as well as new sulfonylureas with different modes of action (9).

Insulin. Exogenous insulin replacement is necessary for type I diabetes to avoid ketoacidosis and maintain life. It is used for the type II diabetic who cannot be satisfactorily controlled by other treatments. Insulin is the treatment of choice for pregnant diabetic women and for patients with acute stressful situations such as surgery, systemic infections, and, of course, ketotic and nonketotic diabetic coma.

Troglitazone. This product, debuting in 1997, acts directly to improve cell response to insulin (lowers insulin resistance). In field trials, insulin requirements in type II diabetes have been reduced markedly and even eliminated in a significant percentage of cases. Dosage is 200–600 mg per day.

Many types of insulin are available. The animal insulin prepa-

Table 31.6.**Common human insulin preparations and time course of action.^a**

Insulin Preparation	Onset	Peak	Duration
Short acting			
Humulin R.	30 min	2–3 hr	6 hr
Novolin R.	30 min	2–3 hr	6 hr
Intermediate acting			
Humulin N.	2–4 hr	7–9 hr	14–24 hr
Novolin L.	3–4 hr	8–10 hr	16–24 hr
Long acting			
Humulin U (Ultralente)	5–8 hr	8–20 hr	20–30 hr

^aConsiderable variation is found in individuals.

rations, pork and beef, have to a large extent been replaced by human insulins. By common usage they are classified as short-, intermediate-, and long-acting preparations. Table 31.6 lists some of the insulins commonly used in the United States. There is individual variation in absorption, peak actions, and duration of effect. The site of injection, physical activity, local tissue influences, and the mixture of insulin can influence the rate of absorption and duration of action of insulin.

A newly diagnosed type I diabetic usually presents with marked hyperglycemia. Small doses of regular human insulin ranging from 3 to 10 units may be given subcutaneously or intramuscularly every 4 hours if the patient is alert and active. Glucose levels can be monitored by finger sticks every 2 to 4 hours initially until stabilization occurs. If ketosis or glucose levels exceed 300 mg/dL, deliver insulin intravenously. An effective method is continuous intravenous infusion of low concentrations of insulin. A liter of 0.5 normal saline containing 100 units of regular insulin dripping at a rate of 10 mL/hour provides 1 unit per hour. If the rate is increased to 20 mL/hour, 2 units of insulin are provided. The dose can easily be adjusted depending on the glucose monitoring.

How does one determine the insulin regimen when conditions are fairly stable? An estimate of the daily insulin requirement is 0.5 U to 1.0 U per kg body weight. A person weighing 60 kg might begin 30 U of insulin daily. A minimum of two injections per day is preferable to only one injection. Begin with about two-thirds of the total daily insulin dosage in the morning and one-third before dinner. A mixture of 2 parts intermediate-acting insulin to 1 part short-acting insulin is a reasonable initial regimen.

The 60 kg patient would receive 14 U of NPH or Lente mixed with 6 U of regular in the morning and 6 U of NPH or Lente mixed with 3 U regular in the evening. By self-monitoring of blood glucose, adjustments can be made over several days. The axiom to “start low and go slow” is a wise one. Premixed combinations, for example, Novolin 70/30 containing 70% intermediate-acting insulin and 30% short-acting are commercially available.

The insulin regimen should fit the habits and lifestyle of the individual rather than living around the insulin doses. Trial and error may suggest that three injections a day is preferable. Mixed doses before breakfast, a short-acting insulin before dinner, and intermediate-acting insulin at bedtime is effective in many patients who have difficulty on two doses a day. Another regimen is short-acting insulin before each meal and ultra Lente once a day to provide a basal level of insulin over the 24-hour period. Continuous subcutaneous insulin infusion by an insulin pump is another option that some diabetologists use. There are clinical trials using implantable insulin pumps, which provide a constant basal level of insulin, and a bolus of insulin programmed to coincide with meals. An intravenous or peritoneal route is used, and the proper delivery algorithm can closely mimic natural physiology of insulin dynamics.

Self-monitoring of blood glucose and glycosylated Hgb determinations represents major advancements in improving glycemic control. Patients can learn to make minor adjustments in insulin doses. They must be able to recognize hypoglycemic reactions, and understand rebound hyperglycemia (Somogyi phenomenon). They must learn to rotate injection sites and assure sterile conditions. A large variety of blood glucose meters are available. Advise patients to measure glucose levels as often as necessary to achieve the best control possible.

Complications of Diabetes

It is convenient to think of the complications of diabetes mellitus as acute or chronic. The acute complications are hypoglycemia, diabetic ketoacidosis, and hyperosmolar coma. The major chronic complications include retinopathy, nephropathy, neuropathy, and atherosclerosis. There are other chronic complications, which are less frequently observed, such as dermopathy, Charcot's joints, and chronic infection due to compromised circulation or impaired immune responses.

Hypoglycemia

This is common in type I and insulin treated type II diabetics. It is less frequent in patients treated with sulfonylureas. Severe episodes may be associated with cerebral damage and death.

The clinical manifestations of hypoglycemia arise from catecholamine release or glucopenia of neural tissue. The secretion of epinephrine produces sweating, tremor, irritability, hunger or nausea, tachycardia, increased systolic blood pressure, and pallor. Some type I diabetics lose the ability to recognize these symptoms, especially if control is poor. Beta-blocking medications can also mask all of these symptoms except increased perspiration. If glucose falls to very low levels, usually below 50 mg/dL, neurologic symptoms and signs occur. These include confusion, uncharacteristic behavior, headaches, syncope, loss of memory, seizures or coma. The diagnosis is usually suspected by the patient or family member or can quickly be confirmed by determining glucose by a finger stick. The cause may be excessive insulin, skipped or late meals, or exercise. Most patients notice early symptoms and eat rapidly absorbed carbohydrates: candy or orange juice. Intravenous glucose is the treatment of choice for comatose patients. An individual who is prone to develop hypoglycemia should have glucagon 1 mg ampules for a family member to inject subcutaneously. Some diabetics carry "instant glucose," which can be placed in the buccal mucosa if food cannot be swallowed in a timely fashion.

Diabetic Ketoacidosis

This is a serious complication associated with a mortality rate of 5% or more. Fortunately, it is not as common as it was several decades ago because of better education and home glucose monitoring.

Ketoacidosis is due to insulin deficiency. A relative or absolute increase in glucagon secretion contributes to the metabolic affects. It may be the presenting feature at the time of diagnosis, or result from omission of insulin, severe infection, or a catastrophic event such as stroke or myocardial infarction. The patient is dehydrated, weak, polyuric, thirsty, lethargic, or comatose. The fruity odor of ketones, deep and prolonged (Kussmaul) respirations, tachycardia, hypotension, palpable liver, tender abdomen, and warm dry skin are commonly present. The diagnosis can be quickly confirmed by laboratory tests. The serum glucose level

ranges from 200 mg/dl to extremely high levels (up to 800 mg/dL); however, in the great majority, glucose levels in DKA are in the 300 to 600 mg/dL range. DKA at levels below 300 mg/dL are unusual, while levels above 800 mg/dL may denote pre-existing renal insufficiency. Acetoacetate (AcAc) and beta-hydroxybutyrate (BOH) accumulate and produce acidosis. Lactic acid may also rise if hypoxia is present. The testing tablet or strip for ketones measures only AcAc, so some caution is needed in interpreting ketones. BOH must be oxidized to AcAc. If hypoxia exists, the ketones may reflect erroneously low values by sodium nitroprusside powder or Acetest tablet. If the ketone reaction is strong in diluted serum, either diabetic or alcoholic ketoacidosis is virtually certain to exist. Starvation ketosis rarely gives a strong reaction past the undiluted serum. Serum bicarbonate is characteristically below 20 mmol/L and the arterial pH is low. The potassium level may be low, normal, or high even though total body stores are always diminished in ketoacidosis. The acidosis facilitates intracellular K^+ to enter the extracellular fluid, so initially the level is elevated. If hypokalemia is found initially, severe total body K^+ losses probably already occurred. There are losses in other electrolytes also in ketoacidosis.

The urgent goal of therapy is to correct life-threatening problems. Try to determine what precipitated the ketoacidosis, especially critical conditions such as myocardial infarction, stroke, or pancreatitis. Begin rehydration with normal saline (0.9%) or half normal saline (0.45%). Infusion of 1 liter over 1 to 2 hours begins to relieve dehydration and helps restore a pressure. Insulin should simultaneously be given, intravenously. We prefer to give 10 to 25 units of regular insulin as a bolus and then begin continuous low-dose intravenous infusion of insulin as described in the section on insulin therapy. Approximately 10 U per hour is used for the first few hours, and then adjusted by monitoring the proper laboratory and clinical signs. As glucose concentrations decrease to about 250 mg/dL, 5% glucose solutions can be added to avert hypoglycemia. Potassium replacement is necessary, but the timing is important. Be certain that there is urine output, and that hyperkalemia is beginning to decrease. Then add approximately 20 to 30 mEq of potassium as neutral phosphate to each liter of fluid until potassium is replenished. Ringer's lactate can be given after initial hydration with saline. An alert patient who is not nauseated may begin to sip on juices,

or take small amounts of broth. There is nothing more dramatic in medicine than a comatose, severely dehydrated, almost dead patient with diabetic ketoacidosis responding over a few hours to fluids, insulin and electrolytes. Careful observations by a knowledgeable clinician monitoring glucose, potassium, ketones, and pH about every 2 to 4 hours during the initial therapy are critical for a successful outcome. Sodium bicarbonate is only necessary if the arterial pH is below 7.0. Its use can cause a paradoxical acidosis in the cerebrospinal fluid or change the dissociation of oxygen from oxyhemoglobin so as to impede delivery of oxygen to tissues. It is helpful to use a flow chart that lists treatments, laboratory data, and clinical observations.

Hyperosmolar Coma

This complication is manifested by marked hyperglycemia (600 to 1000 mg/dL), increased serum osmolality, and little or no ketoacidosis. It is associated with severe dehydration, various neurologic signs, and coma. Hyperosmolar coma tends to occur in elderly type II diabetics, but may occur in type I diabetics as well.

The pathogenesis of the marked hyperglycemia without ketoacidosis is unclear. In some patients a small amount of insulin secretion remains, and it may be sufficient to inhibit lipolysis and ketogenesis. Free fatty acids are lower than those in diabetic ketoacidosis. Hyperosmolality may also inhibit lipolysis (10).

The mortality rate for hyperosmolar coma is approximately 50%, probably because of the severity of underlying illnesses that precipitate it. Stroke, infection, myocardial infection, medications such as diuretics, beta blockers, or steroids, or excessive simple carbohydrates intravenously or orally can initiate the disorder. The profound diuresis and dehydration result in diminished urinary output and azotemia.

The serum osmolality is commonly above 350 mOsm per liter. It may be estimated by the formula:

$$\text{mOsm} = 2(\text{Na}^+ + \text{K}^+) + \frac{\text{Glucose (mg/dL)}}{18} + \frac{\text{Bun (mg/dL)}}{2.8}$$

Immediate treatment is critical. Normal saline is the preferable fluid to initiate treatment to support the blood pressure. Then 0.5 normal saline chloride can be used. Insulin is given intravenously to avoid the problem of absorbing it from subcutaneous tissue in a hypotensive dehydrated person. A regimen similar to that in ke-

toacidosis can be used, but ordinarily less insulin is needed than in diabetic ketoacidosis. A gradual decrease in glucose concentration may be helpful in preventing cerebral edema during treatment. It is necessary to thoroughly search for and treat precipitating causes. A few patients may not need exogenous insulin after recovery.

Chronic Complications

Today, the major problems of diabetics are those of long-term complications: retinopathy, nephropathy, neuropathy and atherosclerosis. The link between diabetes and the “triopathies” are indeed close and direct. The Diabetes Control and Complication Trial (DCCT) has persuaded even the most critical observers that excellent glycemic control impacts these complications favorably (6). On the other hand, diabetes appears to be a risk factor in atherosclerosis much like smoking or hypertension is. Diabetes has adverse effects on lipids, clotting, and structural changes on blood vessels that contribute to atherogenesis or the catastrophic event itself. It is in dealing with these chronic complications that primary-care physicians find expert consultative help most useful.

Diabetic Retinopathy

This is the leading cause of blindness and is responsible for more than 50% of new cases each year in the United States. Approximately half of all diabetics develop some changes consistent with retinopathy after 10 years of the disease, and it increases with duration of diabetes. It is more common in type I diabetics, but because type II diabetics are more numerous, retinopathy is observed regularly in both types of diabetics. Diabetes also accelerates cataract formation. The physician should examine the fundi of diabetics at each routine visit. Annual examination by an ophthalmologist is recommended when a lesion is seen or after 5 years of known diabetes.

Background retinopathy is the early stage of diabetic changes on ophthalmologic examinations. Microaneurysms, intraretinal dot hemorrhages, hard exudates, and cotton-wool exudates are representative lesions. This stage is usually not associated with visual loss and may not progress. The “soft” or cotton-wool exudates are small infarcts of the inner retinal layers. Proliferative diabetic retinopathy is the stage that is of concern. New vessel proliferation occurs on the retinal surface and can extend to the posterior

vitreous. Hemorrhage, scarring, and retinal detachment are events that impair vision significantly. Figure 31.1 shows examples of background (A) and proliferative (B) retinopathy.

Photocoagulation is effective in the treatment of retinopathy. Lesions caused by laser treatment diminish the hypoxemic stimulus for neoproliferations. Vitrectomy is utilized for scarring

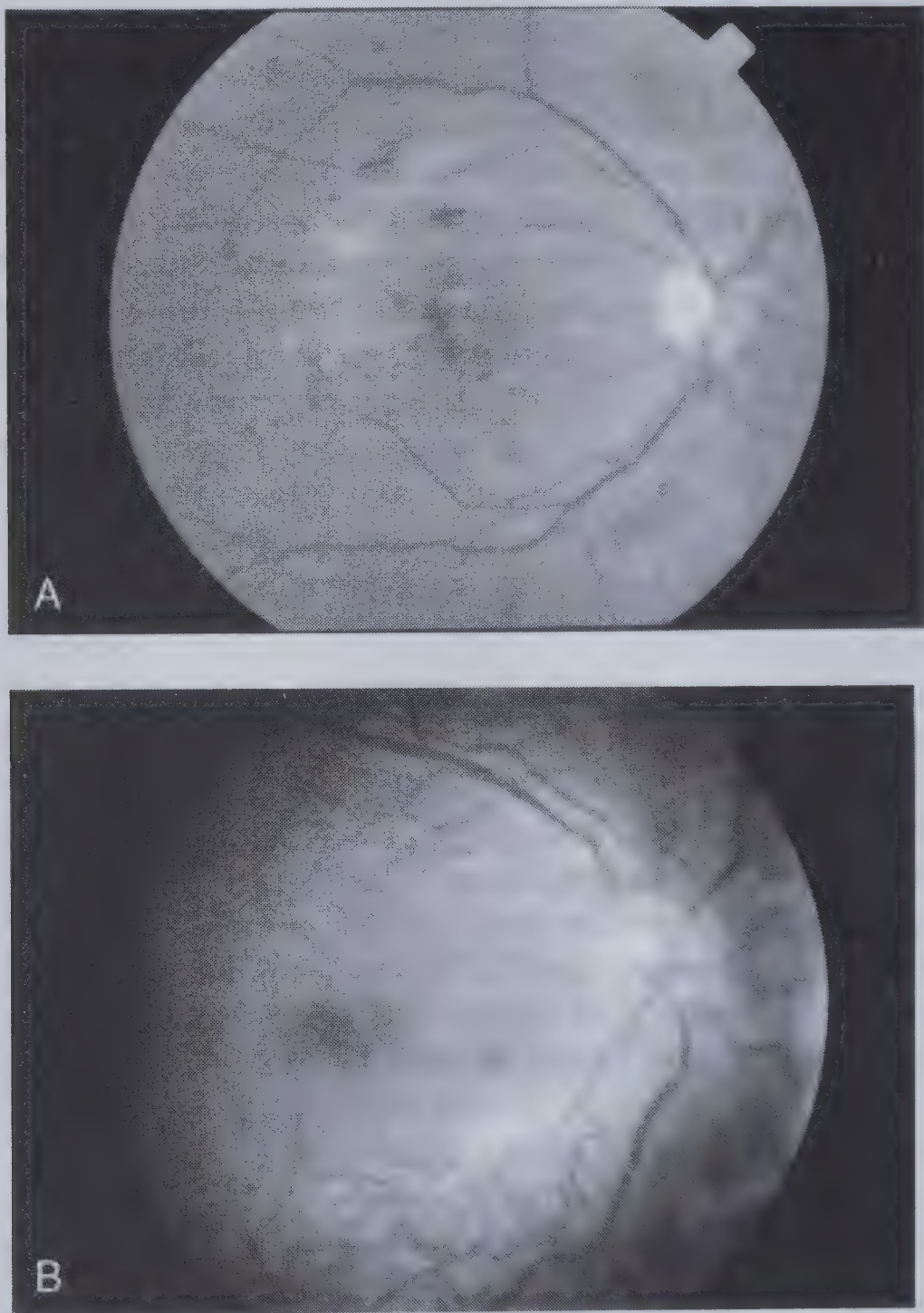


Figure 31.1 **A.** Nonproliferative (background diabetic) retinopathy; microaneurysmal changes, blot hemorrhages, and exudate. **B.** Proliferative diabetic retinopathy; neovascularization of the optic nerve, head and focal zones of neoproliferation along the superior-temporal vascular arcade. (Reprinted with permission from Dr. Alice Epitropoulos, Ohio State University.)

and hemorrhage that do not resolve. The DCCT showed that intensive treatment to control glycemia reduced the risk of meaningful retinopathy by 76% (6). Control of hypertension is also beneficial.

Nephropathy

This complication of diabetes occurs in about one-third of type I diabetics and at least 15% of type II diabetics. Some families with diabetes have a high proportion of members who develop nephropathy, while other families have very few members with it. Kimmelstiel-Wilson nodules, although well known and most specific for diabetic renal disease, are not as common as the diffuse pattern of basement membranes and mesangial thickening.

The kidneys of diabetic individuals are enlarged initially and have above-normal glomerular filtration rates (GFR). Microalbuminuria, (excretion of 30 to 300 mg per day) is the next stage. It is not detected in routine tests for urinary protein, thus 24-hour quantitative measurements for albumin should be done annually after the diagnosis of diabetes has been present for 5 years. When albumin excretion exceeds 300 mg per day, the GFR begins to diminish at a relatively predictable rate. The nephrotic syndrome may appear. Eventually azotemia signals the presence of renal disease and renal failure. Diabetes is responsible for approximately one-third of the cases of end-stage renal disease.

The DCCT showed that improved glycemic control delays the progression of renal disease (6). If hypertension is present, control of the blood pressure is remarkably effective in slowing the progression of the disease. Angiotensin-converting enzyme (ACE) inhibitors may have a protective influence, but correction of blood pressure by various antihypertensive agents seems to be the important element. A low protein intake is advantageous once azotemia develops. The diabetic patient should probably begin hemodialysis or undergo renal transplantation when the creatinine reaches about 5.0 mg/dL, somewhat earlier than in other renal diseases. Azotemia and uremia adversely affect vascular disease and other complications in long-standing diabetes. Simultaneous renal and pancreas transplantation is becoming an increasingly popular procedure. Overall results have been gratifying for renal transplantation, alone, or in combination with pancreas transplantation.

Diabetic Neuropathy

This complication may be present at the time of diagnosis of diabetes or, more usually, occurs with increasing duration of the disorder. It is a troublesome problem resulting in a great deal of discomfort and morbidity. A useful classification for clinical use includes 1) peripheral polyneuropathy, 2) mononeuropathy, and 3) autonomic neuropathy.

The pathogenesis of diabetic neuropathy is better understood than it was a few years ago. Evidence in recent years suggests that both metabolic and ischemic factors interact to produce the clinical neuropathies. The acute abnormalities that accompany marked hyperglycemia are reversible, but prolonged damage by metabolic changes result in permanent changes. Metabolic abnormalities include intracellular accumulation of sorbitol, myoinositol depletion, reduced ATPase activity, and glycosylation of proteins in the nerve. Ischemic causes of neuropathy are implicated in mono-neuropathies and involve the microvascular circulation.

Peripheral polyneuropathy, the most common type, involves the lower extremities in a symmetrical distribution. Numbness, pain, hypesthesia, and increased sensitivity to pressure or touch, are common symptoms. An early sign that almost always accompanies diabetic neuropathy is loss of the Achilles tendon reflex. Severe pain may persist for months, but is usually self-limited. Mononeuropathy tends to occur suddenly involving a single nerve or plexus. Bell's palsy, lateral rectus paralysis, or ptosis of the lid are examples of involvement of cranial nerves. Mononeuropathies almost always resolve gradually over a period of weeks. Autonomic neuropathies cause a variety of symptoms and signs. Some examples are silent myocardial infarction, orthostatic hypotension, delayed gastric emptying, diarrhea, impotency, and retrograde ejaculation. Diagnosis of the neuropathies can be confirmed by electrophysiologic studies of the affected nerves.

Various treatments for neuropathies have been tried, but, in general, have been disappointing. Strict control of glycemia is associated with reduction of the risk of meaningful neuropathy by about 60% (6). Mild analgesics are frequently sufficient to ease pain, and amitriptyline 25 or 50 mg at bedtime is often helpful. Metoclopramide or propulsid is helpful for gastroparesis. Penile implants, vacuum devices, and injections into the penis have all

been used successfully to improve erectile function. An interesting approach to treating diabetic neuropathy has been reported using essential fatty acids (11). Investigators identified a deficiency of gamma linolenic acid (GLA) formation from linoleic acid in diabetes. In a multicenter trial patients were given GLA in the form of 500 mg, evening primrose oil, 12 capsules per day for 1 year and compared with patients taking placebo. Evaluation of neurophysiological and thermal sensitivity parameters showed significant improvements in the experimental group as compared with the placebo group. Evening primrose oil capsules are widely available in the United States in health food stores. Although encouraging, these results should be confirmed. Maintaining excellent glycemic control is the treatment of choice at this time.

Macrovascular Disease

Not unique to diabetics, this nevertheless occurs more extensively and earlier in life as compared to nondiabetics. Coronary heart disease, stroke, and peripheral vascular disease are more frequent in diabetics as compared with nondiabetics and represent the major causes of mortality. Atherosclerosis is a multifactorial disease, and diabetes is one of the risk factors. Diabetes has a direct influence on the atherosclerotic process, but it also has a strong impact on hyperlipidemia and hypertension, both important risk factors.

The diabetic state influences lipid metabolism in several ways. Insulin is a lipogenic hormone. It is required for carbohydrate metabolic products to be converted to fatty acids and triglycerides. In type II diabetics, insulin resistance is common, and insulin levels are frequently elevated in patients who do not have islet cell failure. Thus, the normal physiologic effects of insulin are exaggerated and triglyceride synthesis is enhanced. Hypertriglyceridemia is relatively common in type II diabetics as is the usual reciprocal relationship of diminished HDL cholesterol. Both abnormalities contribute to atherosclerosis. Also, the diabetic state adversely influences LDL cholesterol, probably by glycosylating proteins in LDL cholesterol and making them more difficult to be removed by receptors. Oxidized LDL cholesterol is considerably more atherogenic than native LDL cholesterol, and diabetes adversely affects this process.

The combination of diabetes and hypertension is common, and both conditions result in acceleration of atherosclerosis. Diabetes predisposes patients to hypertension in two ways: by affecting renal function directly in relation to hyperglycemia and in type II diabetics, by the effects of hyperinsulinemia. Hypertension prevalence increases with duration of diabetes and is correlated with albuminuria. Some antihypertensive agents such as thiazide diuretics and the nonspecific beta blockers may play a role in inducing insulin resistance or directly raising glucose levels in susceptible individuals. Hypertension is approximately twice as frequent in a diabetic as compared with a nondiabetic population (12). The hypertension is likely to be associated with low renin levels and increased fluid volume.

Syndrome X is a condition described by Reaven (13) representing a cluster of metabolic abnormalities found in individuals who have a predisposition to develop coronary disease. Table 31.7 lists those metabolic abnormalities. Hyperinsulinemia due to insulin resistance may be the underlying abnormality responsible of these associated risk factors for atherosclerosis.

Diabetics must not only be concerned with achieving excellent glycemic control, but amelioration of the risk factors for atherosclerosis as well. Hypertension must be treated early and effectively. Encourage patients to stop smoking. Lipid levels, especially total and HDL cholesterol should be determined initially and followed at intervals. The ADA diet is designed to address lipid abnormalities as much as it is to lower glucose levels. Excellent lipid-lowering drugs are available to correct dyslipidemia.

Other long-term complications occur in diabetics, but are less common than those described above. Diabetic dermopathy occurs in many insulin-dependent diabetics as shin spots. They are atrophic lesions usually on the lower extremities, and heal

Table 31.7.
Syndrome X.

Insulin resistance
Hyperinsulinemia
Glucose intolerance
Hypertriglyceridemia (VLDL)
Decreased high density lipoprotein cholesterol
Hypertension
Aggravated by obesity

with a thin nonpigmented scar. Necrobiosis lipoidica diabetico-rum also occur on the shins, but they are ulcerations and tend to be necrotic. The lesions should be gently cleaned with warm washes, and an antibiotic-steroid cream applied. Saran wrap can be applied to cover these lesions at night. Foot care is a high priority in diabetic education. Every routine clinical examination should include an inspection of the bare feet.

Managing the Care of Diabetics

There is increasing interest in managed care of chronic diseases. Medical care guidelines are being developed by national organizations and local experts. Table 31.8 summarizes those elements of care for the diabetic component of patient follow-up.

Intensive diabetic treatment with frequent home glucose mon-

Table 31.8
Guide for follow-up care.

Diabetes Mellitus Type I and II		
Recommended evaluation and intervention to prevent and detect complications after initial diagnosis established.		
	Insulin Requiring	Noninsulin Requiring
Element of Care	Frequency Every	
Comprehensive evaluation	12 months	12 months
Routine evaluation	3 to 6 months	6 months
Foot examination	3 to 6 months	6 months
Blood pressure	3 to 6 months	6 months
Eye examination-dilated pupils	12 months	12 months
Nutrition evaluation and counseling	12 months	12 months
Preconception counseling and establishment of normal glycemic control for women planning pregnancy	As needed	As needed
Laboratory tests after initial assessment and diagnosis		
Home glucose monitoring	Daily (1 to 4 times)	As prescribed
Hgb A1C	3 to 6 months	6 months
Urinalysis, multi-stick	3 to 6 months	6 months
Fasting lipid profile	12 months	12 months
Lytes, CBC, creatinine	12 months	12 months
24-hour urine albumin	12 months	12 months

itoring does not cause a deterioration in the quality of life of most compliant diabetic patients (14). General recommendations designed to address six complications are outlined in Table 31.9 (15).

Diabetes and Pregnancy

Diabetes has an extremely important impact during a brief period of time in life—the 9 months of pregnancy. Like other physiologic stresses, pregnancy influences carbohydrate metabolism by increasing insulin resistance and serum glucose in susceptible individuals. If good control is not maintained, maternal and fetal complications may occur.

During early pregnancy various hormonal changes occur. Human placental lactogen promotes insulin resistance. Thus, the mother may develop glucose intolerance or diabetes during pregnancy, or if she is a known diabetic, may become worse.

Table 31.9.

Recommendations for management of diabetes to detect and prevent the common complications.

1. *Retinopathy:* Annual visual examination through a dilated pupil, with thorough vitreous and retinal examination, including stereoscopic examination of the macula.
2. *Nephropathy:* Annual measurement of protein excretion and creatinine clearance, careful monitoring and treatment of blood pressure, limitation of protein intake when microalbuminuria has been detected. Referral to diabetologist or nephrologist when renal impairment is diagnosed.
3. *Acute complications:* Develop individualized treatment plans to instruct and encourage patients at risk for hypoglycemia and hyperglycemia to perform self blood glucose monitoring and maintain contact with their health-care team.
4. *Macrovascular:* If a patient smokes, prescribe a program to stop smoking; monitor blood pressure 4 times a year, measure triglycerides, total cholesterol and high density lipoprotein cholesterol, adjust diet and exercise program as needed.
5. *Feet:* Patient's legs and feet should be examined at every regular visit. A neurologic and vascular examination should be done annually. If abnormalities are detected, a qualified specialist should be consulted.
6. *Pregnancy:* Women with known diabetes should have preconception counseling and examination. All women not known to have diabetes should be screened between 24 and 28 weeks with plasma glucose 1 hour after 50 gm of oral glucose.

Stillbirths were relatively common in the past, occurring in about 20% of diabetic pregnancies. Good glycemic control has decreased this problem, but the rate is still higher than in non-diabetic pregnancies. Congenital malformation occurs four or five times more frequently than in controls. A striking example is the fact that sacral agenesis or caudal dysplasia is found 200 times more frequently in offspring of diabetic mothers as compared with those born to nondiabetics. Hypoglycemia occurs in the majority of newborns of diabetic mothers versus about 2% of infants in general. Infants weighing 4000 grams or more (macrosomia) are still quite common. Both of these latter conditions are improved if glycemic control is achieved during the gestational period. Increased maternal glucose levels cross the placenta and stimulate islet cell hyperplasia and increased insulin secretion in the infant. The potent anabolic effects of insulin result in increased storage of fat, protein and glycogen in the fetus.

Hypokalemia, hyperbilirubinemia, and a variety of central nervous system anomalies also may be present (16). The mother is also adversely affected, suffering from increased frequency of ketoacidosis, preeclampsia, and spontaneous abortions.

Good obstetric and diabetic management requires frequent and careful follow-up by the primary-care physician, obstetrician, and diabetologist. All pregnant women should be screened for glucose intolerance between the 24th and 28th week by giving 50 gm oral glucose and determining the glucose level 1 hour later. If the glucose exceeds 140 mg/dL, a 3-hour glucose tolerance test should be done using 100 gm oral glucose. An oral glucose load of 100 gm is ingested, and if two of the following values equal or exceed 105, 190, 165, and 145 mg/dL at 0, 1, 2, and 3 hours, gestational diabetes exists.

Glycemic control must be near normal during pregnancy because dramatic improvements in the mother and fetus are possible. The patient's ages of onset of diabetes, duration, and presence of vascular disease influence the outcome of the pregnancy. Gestational diabetics should be tried on dietary control, using 30 to 40 kcal per kg ideal body weight. If normal glucose levels are not achieved in the fasting state and after meals, insulin, not oral hypoglycemic agents, should be used. The goal is fasting glucose levels of approximately 100 mg/dL and 2 hours post prandial values of approximately 120 mg /dL. Hypoglycemia should be avoided, although ketoacidosis is more dangerous to the fetus.

Home glucose monitoring before meals and at bedtime and at least twice a day insulin injections of intermediate- and short-acting insulin are necessary. Supplemental regular insulin injections can be given before meals. Continuous subcutaneous insulin infusion by pump is quite acceptable when multiple injections are not meeting the goals. Patients are really quite motivated, and good control can be achieved! Glycosylated hemoglobin determinations should be obtained at regular intervals to confirm that control is adequate.

The timing of delivery is now similar to that of the nondiabetic. Testing is available to assess fetal condition and to avoid premature intervention. The contraction stress test predicts fetal survival for 1 week. The nonstress test, and the biophysical profiles, along with monitoring of fetal activity and heart rate, are reliable tools available to the obstetrician or family physician for fetal surveillance and timing of delivery (17). During labor it is customary to monitor fetal heart rate continuously. A neonatologist should be present at delivery to care for the infant and treat conditions such as hypoglycemia. There is a relatively abrupt decrease in maternal insulin requirements after the placenta is delivered. Follow-up diagnostic tests should be performed in gestational diabetics because of the increased risk of having permanent diabetes.

Future Directions

Exciting new information and discoveries are reported almost daily in diabetes. Powerful genetic and biologic tools to elucidate the mechanisms that are operative in type I and type II diabetes are available. Prevention of type I diabetes may soon be possible. Pancreas transplantation is increasingly successful, and islet cell transplantation may soon be commonplace. New oral agents have been introduced and new ones are on the horizon. The rationale of excellent glycemic control has been strengthened based on sound scientific clinical trials. The future does indeed look promising for the many people living with diabetes mellitus.

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Thyroid Problems in Primary Care

David R. Rudy and Manuel Tzagournis

INTRODUCTION AND PHYSIOLOGY

Thyroid disorders are the second most common endocrine illness seen in primary care after diabetes. Abnormalities are manifested by excessive or deficient secretion of hormone, enlargement of the gland (goiter), inflammation, and tumors, benign or malignant.

Tetraiodothyronine (T₄) and tri-iodothyronine (T₃) are formed from monoiodotyrosine and diiodotyrosine and stored as thyroglobulin in the follicles. Secreted hormone leaves the gland in a ratio T₄/T₃ = 10:1. Thyroid hormones in plasma are bound mostly to thyroid binding globulin (TBG) and a prealbumin binding protein. One iodine atom is removed from T₄ in peripheral tissue to produce the active form, T-3. TBG is elevated by estrogen, birth control pills, pregnancy, and some liver diseases; and diminished by androgens, glucocorticoids, the nephrotic syndrome, and major systemic illnesses.

Thyroid hormones are produced in response to stimulation by thyrotrophin (thyroid stimulating hormone, TSH) from the pituitary, and production subsides when TSH subsides. Hypothalamic thyrotropin releasing hormone (TRH) stimulates TSH release in response to lowered T₄ or T₃ concentrations, while somatostatin, also from the hypothalamus, inhibits TSH secretion in response to heightened hormone levels. TSH acts to increase iodine uptake by the thyroid and to accelerate all steps of synthesis and release of hormones.

Thyroid Function Tests

Specific and sensitive tests to measure free T4 or T3 levels are now available. Less direct methods include measurement of the total circulating concentrations of T4, T3, and reverse T3. Since bound and unbound fractions of the hormones are included in the measurement, a simultaneous estimate of the thyroid-binding proteins must be made to interpret the results properly. The direct measurement of T3 by radioimmunoassay is helpful in certain circumstances, such as T3 thyrotoxicosis, when T4 levels are normal. Normal T3 concentrations range from 70 to 190 $\mu\text{ng/dL}$ and free T4 levels are 5 to 11 $\mu\text{gm/dL}$ (1).

T4 levels are elevated in hyperthyroidism and low in hypothyroidism. In situations of elevated TBG, such as pregnancy or exogenous estrogens, the bound and unbound T4 may be spuriously elevated. Thus, a test for protein bound hormone is ordered at the same time.

Serum TSH Concentrations

The advent of TSH measurement by radioimmunoassay has given clinicians the most sensitive test of thyroid function. Its elevation can diagnose arcane hypothyroidism in the absence of clinical or other laboratory evidence. The sensitive TSH measurement is necessary even in obvious clinical hypothyroidism to differentiate primary versus secondary hypothyroidism. Treatment of secondary hypothyroidism without addressing the remaining pituitary axis can precipitate adrenal insufficiency.

Sensitive TSH can signal hyperthyroidism as well, whether endogenous or exogenous. It is useful in following the appropriateness of therapeutic thyroid hormone dosage both in replacement therapy or in goiter suppression. The normal range of serum TSH is 0.5 to 5 mU/L, in most laboratories.

Thyroid Radioactive Iodine Uptake and Scanning

This is a direct physiologic test of thyroid uptake using tracer doses of ^{123}I , which, by virtue of its short half-life delivers less radiation than does ^{131}I . Normally 5% to 25% of radioactive iodine is taken up by the thyroid in 24 hours. An elevated uptake is seen in hyperthyroidism, some situations of iodine deficiency, situations of metabolically blocked hormone synthesis, or in conditions of hypoproteinaemia resulting in decreased binding proteins. Diminished uptake is

associated with hypothyroidism, thyroiditis, excessive iodine intake, exogenous thyroid (including factitious hyperthyroidism) or circulating anti-thyroid agents. ^{123}I uptake testing should be done prior to treatment of thyrotoxicosis with therapeutic ^{131}I in order to confirm adequate uptake of the therapeutic iodine.

An image of the thyroid can be obtained by external scintiscanning with a rectilinear scanner or stationary camera after a tracer dose of ^{123}I . ^{99}Tc (pertechnetate) can be used for such a scan as well. Areas of increased or decreased function signal size and location of the gland and identification of nonfunctioning ("cold") nodules, which are more likely than functional nodules to be cancerous. Total body scans with ^{131}I are used to identify metastatic thyroid cancer.

Ultrasonography

This is a noninvasive method that has improved thyroid imaging. Cystic lesions are sonolucent while solid lesions are echogenic.

Thyroid Releasing Hormone (TRH)

TSH is measured 30 minutes after TRH; 400 μgm is infused intravenously. The peak value is elevated in primary hypothyroidism from the normal range of 5 to 30 mU/L and tends to be flat in hyperthyroidism. It allows distinction between pituitary and hypothalamic secondary hypothyroidism. A subnormal response denotes pituitary failure.

Serum Thyroglobulins

Measurement is of value for the follow-up of people treated for thyroid cancer. Elevation is noted in well-differentiated thyroid carcinoma and in hyperthyroidism, many goiters and thyroiditis. Quantification of serum thyroglobulins allows follow-up of those conditions as well.

Thyroid *microsomal* or *thyroglobulin antibodies* are elevated in Hashimoto's thyroiditis, Grave's disease, and transient thyrotoxicosis due to chronic autoimmune thyroiditis.

THYROTOXICOSIS

Thyrotoxicosis (hyperthyroidism) is much more common in women than in men. Grave's disease is the most common form of

thyrotoxicosis in the United States, with a lifetime incidence of 0.4% and a female:male ratio of 10:1, translating to a prevalence of 2.2% in females and 0.2% in males. Other causes of hyperthyroidism are toxic multinodular goiters, thyroid adenomas, thyroiditis, autonomous secretion of TSH, ectopic thyroid tissue, and exogenous thyroid intake (iatrogenic or factitious thyrotoxicosis).

Grave's Disease

This is an autoimmune disease in which IGG reacts with the TSH receptor of the thyroid cell and mimics TSH action. Thus, an antibody stimulates the thyroid gland to elaborate hormone in excess. The IGG antibody is measurable as thyroid stimulating immunoglobulin (TSI) or TSH-displacing antibody, and is often elevated in Grave's disease. These antibodies may be mainly inflammatory (autoimmune thyroiditis), stimulatory (Grave's disease), or blocking of TSH receptor binding to produce hypothyroidism. Besides those clinical findings common to all thyrotoxicosis, there are some manifestations unique to Grave's.

Multinodular Toxic Goiter (MTG)

This entity is a form of primary hyperthyroidism in which areas of the thyroid gland, for unknown reasons, become autonomous and produce excessive hormone. It is preceded by nontoxic nodular goiter, in which the gland develops histologic and functional heterogeneity, wherein active areas gradually become autonomous. This disease is less severely thyrotoxic and less common than Grave's disease. The T₃, T₄ and ¹²³I uptake are likely to be mildly abnormal in contrast to Grave's disease. It occurs far more frequently in women than in men, but because of the indistinct taxonomy and often mild nature of the disease, the prevalence is not well established. During the nontoxic phase, exposure to increased amounts of iodine by ingestion, or by ingestion of goitrogens in grass or water contaminants may precipitate thyrotoxicosis rapidly rather than gradually. The toxic phase occurs in the great majority, after the age of 50. By definition, these nodules or adenomas are not responsive to suppression of TSH and do not involve stimulatory antibody. The active nodules take up radioiodine, while surrounding normal thyroid is inactive due to suppression of TSH. Thus, a scintiscan of the thyroid may show one or two multiple nodules taking up increased radioactivity, while the remainder of the thyroid gland takes up little or none.

Toxic Adenoma

An adenoma of the thyroid (solitary nodule) may also function autonomously and produce excessive thyroid hormones. The toxic adenoma presents as a slowly growing palpable nodule in the gland, in the decades of the 30s and 40s, producing clinical, usually mild toxicity only after it has reached the size of 2 to 3 cm. It may hemorrhage within itself, whereupon toxicity subsides and thereafter, as a "cold" nodule on scintiscan, may mimic carcinoma. In that stage calcification visible on x-ray appears as irregular as opposed to the stippling seen in papillary cancers (2).

Other Forms of Thyrotoxicosis

Subacute thyroiditis may temporarily release excessive thyroid hormone and painless thyroiditis may cause thyrotoxicosis, usually transiently, but sometimes recurrently as well. Rare causes are excessive TSH secretion from a pituitary adenoma or hypothalamic disorder of release of TRH. In these situations, TSH fails to be suppressed despite elevated T3 and T4 levels. Excessive iodine intake can induce hyperthyroidism in people who have either iodine-deficient goiters or nontoxic multinodular goiters. Teratomas may produce ectopic thyroid tissue, and choriocarcinomas or hydatidiform moles may produce thyroid-stimulating factors. Exogenous intake of hormone may occur as factitious or iatrogenic causes of thyrotoxicosis. Patients on thyroid hormone replacement have changing requirements in later years, and thyrotoxicosis may develop gradually. In factitious thyrotoxicosis the patients have high T4 and T3 levels, very low TSH levels, usually a nonpalpable thyroid gland, and virtually no radioactive iodine uptake. This condition would have to be differentiated from transient thyrotoxicosis of thyroiditis.

Clinical Manifestations of Thyrotoxicosis

Common symptoms in thyrotoxicosis are nervousness, heat intolerance, fatigue, increased perspiration, rapid heart rate, weight loss in the face of good appetite, more frequent bowel movements or diarrhea, emotional irritability and weakness. Though many of these symptoms are present in other illnesses, others are highly specific for thyrotoxicosis, such as weight loss despite adequate caloric intake and heat intolerance. Other complaints are thinning or loss of scalp hair, palmar and solar perspiration and erythema, amenorrhea or hypomenorrhea, and

changes in the appearance of the nails. In Grave's disease, the patient might complain of proptosis of the eyes and possibly diplopia. The elderly tend to have symptoms such as angina, heart palpitations, and manifestations of osteoporosis. They may present with "silent" or apathetic thyrotoxicosis.

Systolic blood pressure is high, and the pulse pressure is widened due to the increased stroke volume. There is virtually always sinus tachycardia and possibly atrial fibrillation. The demeanor is one of restlessness and irritability if not anxiety. The skin is warm, velvety, thin and moist. The eyes appear to stare with less blinking. Lid retraction and lag are common with all forms of hyperthyroidism. Infiltrative ophthalmopathy and dermopathy occur only in Grave's disease. Proptosis may be unilateral or bilateral; heterotropia or periorbital edema may be noted.

Areas of vitiligo, if present, are typically symmetrical. The nails might show a distal onycholysis with the leading edge tending to curl upward. There may be digital clubbing or thyroid acropachy. In Grave's disease infiltrative ophthalmopathy usually occurs concurrently with the hyperthyroid state but may precede it, and proptosis may be unilateral or bilateral. Extraocular muscle involvement is manifested by restricted movements, particularly in the superior lateral direction producing diplopia.

Thyromegaly is virtually always appreciable, and gland size may reach 4 to 5 times normal except, of course, in cases of exogenous hormone ingestion or ectopic thyroid production. In Grave's disease the thyroid enlargement is symmetrical and diffuse, often involving a pyramidal lobe. Toxic nodular goiters are irregular and adenomas discretely palpable. A venous hum may be auscultated and sometimes a thrill palpated. The precordium may be active, and there may be a systolic flow murmur. Commonly, there is a tremor, usually fine but sometimes coarse. Deep tendon reflexes are brisk and increased but symmetrical. "Pretibial myxedema" is patchy or confluent erythematous infiltration of the skin, usually in the pretibial area, and when seen in thyrotoxicosis is pathognomonic of Grave's disease. Muscle weakness is not uncommon, especially in Grave's disease, and may be demonstrated by difficulty standing from a squatting position. In the elderly hyperexcitability and tremor may be subtle or absent, but cardiovascular and skin signs are present, as is thyromegaly.

The differential diagnosis includes anxiety, carcinoid syndrome, pheochromocytoma, mitral valve prolapse, all causes of

weight loss, hypoglycemia, and causes of proptosis. CT scan will rule out cavernous sinus thrombosis.

Confirmatory Diagnosis

An elevated free thyroxin index or free T₄ conjoined with a suppressed sensitive TSH concentration is confirmatory of Grave's disease or other primary hyperthyroidism. Isolated T₃ thyrotoxicosis is rare. It is not cost effective to order T₃ studies in screening situations, though sometimes it is economically packaged with T₄ and TSH. Nonsuppression of TSH in hyperthyroid patients signifies pituitary adenoma, antonomous TRH production or ectopic TSH production. Increased radioiodine uptake is found in all forms of primary hyperthyroidism except the transient phase of thyroiditis, during which it is usually low. In factitious hyperthyroidism the uptake is near zero. TSH receptor antibodies are present in Grave's disease.

Treatment of Thyrotoxicosis

There are guidelines for treatment that are accepted by most endocrinologists and are in accord with recent published reviews (3). Propranolol or nadolol, nonselective beta-blocking agents, nearly uniformly produce symptomatic relief in thyrotoxicosis. Propranolol, at a dosage of 10 to 40 mg four times a day, is titrated to suppress tachycardia, tremor, and restlessness. The commonly used definitive treatments each have certain advantages and disadvantages. They are radioiodine, surgery, and antithyroid drugs and are well known from years of use.

Therapeutic Radioiodine

Radioactive iodine (¹³¹I) is the most frequently used treatment in adults in the United States based on its effectiveness and relative economy. Its main disadvantages are the high incidence of hypothyroidism induced and contraindication in pregnancy and in breast feeding. ¹³¹I does not cause cancer nor genetic abnormalities but is contraindicated in pregnancy because it crosses the placenta readily and can be concentrated by the fetal thyroid. Most clinicians avoid its use in children on general principle. Radioiodine-induced hypothyroidism is not a major problem if the patient is compliant in following replacement thyroid therapy. The dose of ¹³¹I ranges between 2 and 20 mC, usually 5 to 15 mC,

by mouth. Dosages estimated to achieve therapeutic effects without permanent hypothyroidism have been impossible to predict so that most clinicians anticipate the need to treat later for hypothyroidism. A 10 mC dose is 90% effective in relieving thyrotoxicosis in Grave's disease. The effects of ^{131}I are significant after 6 weeks and maximal at 3 to 4 months. It may be repeated in 6 months if thyrotoxicosis persists. Pretreatment with antithyroid drugs may prevent exacerbation of thyrotoxic symptoms due to radiation-induced thyroiditis, especially relevant in the elderly or in patients with heart disease. The euthyroid state may be expected in 6 to 8 weeks, and hypothyroidism can occur after many months or years. The required dosage of levothyroxine in patients with postradioiodine hypothyroidism is likely to be lower than the average daily replacement dosage of $1.7 \mu\text{gm/kg}$ ideal body weight (4).

Antithyroid Drugs

These are effective, relatively safe, and achieve symptomatic relief faster than does radioiodine. The most commonly used antithyroid drugs are propylthiouracil (PTU) and methimazole (Tapazole), both of which belong to the thionamide family. They inhibit iodine processing in the synthesis of thyroid hormone as well as peripheral conversion of T4 to T3, the latter in higher dosages. Less than 5% of patients will suffer adverse reactions, the most serious of which is agranulocytosis (0.3 to 0.4%). Agranulocytosis is nearly always reversible with discontinuation early in its onset, for which reason the WBC must be checked frequently in the first several weeks of treatment. Since a relative leukopenia is common in Grave's disease, a baseline count is useful. Other side effects to thionamides include allergies, rashes, hepatic aberrations, musculoskeletal symptoms, and fever; any of these are reasons to discontinue medication. Propylthiouracil is given in dosages of 100 to 300 mg every 12 hours, or methimazole 10 to 40 mg once daily. Larger doses may be required. Patients should be followed initially at 4- to 12-week intervals, depending on the degree of toxicity, until euthyroidism is achieved, at which time the dosage is lowered and the interval of follow-up increased to 3 to 4 months, monitoring the pulse, weight, T4 and TSH. TSH may remain suppressed for months after the T4 has recovered to normal values. The thyroid gland, while usually decreasing in size with therapy, can increase paradoxically if the thy-

roid is blocked excessively and the TSH level increases. PTU is considered safe in pregnant women and is thought to cross the placental barrier less readily than methimazole. However, consultation may be wise in patients with special problems such as pregnancy or childhood thyrotoxicosis. Treatment is continued for approximately 1 year followed by trial withdrawal of the drug. Approximately one-half of Grave's disease patients, especially those with mild cases, will exhibit a natural remission of the disease by then, after which they should still be monitored every 3 to 4 months for 1 year. If the hyperthyroid state relapses, the patient can be retreated or have surgery or radioiodine therapy. The antithyroid drugs are rarely considered as the sole therapeutic agent for Grave's disease in patients older than 40 years.

Surgery

Though employed less often than in the past, surgery has the advantage of the rapidity of cure. This is posed against the disadvantages, which include the surgical assault, and complications, which are risk of recurrent laryngeal nerve damage, hypoparathyroidism, and thyroid storm. Preoperative preparation involves beta-adrenergic blockade, usually with propranolol, often along with antithyroid drugs. Potassium iodide (SSKI) five drops 3 times a day suppresses hormone release and reduces the vascularity. Relapses of thyrotoxicosis postoperatively are uncommon. More often hypothyroidism occurs but at a lesser rate than after ^{131}I therapy.

Adjunctive Therapy

Beta-adrenergic blockade has been discussed. In very mild cases, or transient cases as in thyroiditis, a beta blocker alone may suffice to control the symptoms. Iodine inhibits hormone release and synthesis of T₄. Its use is limited to urgent situations or preoperatively, since the therapeutic effect is lost with chronic use.

Thyroid Storm

This is a dramatic and life-threatening syndrome of exaggerated thyrotoxicity, characterized by combinations of fever, nausea, diaphoresis, tachycardia, or heart failure. It is usually precipitated by stress, surgery, or infection, and may occur in previously undiagnosed or inadequately treated hyperthyroidism. There is no

specific diagnostic means of differentiating storm from other degrees of thyrotoxicity, so that suspicion is reason enough to begin counteractive measures. Rapidly instituted treatment consists of PTU in dosages up to 3 times usual for Grave's disease to inhibit hormone synthesis; iodine as potassium iodide or iopanoic acid (Telepaque) to inhibit release of hormone from the gland; beta-adrenergic blocking drugs to inhibit the peripheral effects of the hormones, and glucocorticoids. Intravenous prednisone, 60 mg per day, is infused to prevent theoretically a relative adrenal insufficiency, as well as to utilize glucocorticoids' action to inhibit peripheral conversion of T4 to T3, but its value in treating storm is unproved. Propranolol is often given intravenously in small doses of 5 to 10 mg every few hours, titrating to the heart rate or rhythm every 6 hours. Oral doses of 40 to 80 mg can be given by mouth or nasogastric tube.

Special Circumstances in Thyrotoxicosis

Pregnant women with Grave's disease are prone to abortions. In addition, neonatal Grave's disease may be present in an infant newly delivered of a mother with Grave's due to autoimmune antibody crossing the placenta. Antithyroid drugs and supportive care of the infant are necessary for several weeks. Conversely, prepartum antithyroid drugs taken by the mother can result in neonatal hypothyroidism, requiring urgent diagnosis and therapy.

Infiltrative ophthalmopathy with muscle dysfunction, diplopia, severe proptosis, or loss of vision is treated by such supportive measures as methyl cellulose tears, and a diuretic such as Diamox several days per week. Prednisone may be prescribed 60 to 80 mg per day, withdrawn over a few weeks, and elevation of the head of the bed at night to diminish edema of the orbit and surroundings. Some regression of the proptosis is possible as the active disease subsides. Less common treatments are orbital irradiation, surgical decompression, and correction of extraocular muscle position. The eye manifestations, after about 2 years, tend to subside.

HYPOTHYROIDISM (RELATIVE AND ABSOLUTE)

This group of disorders includes hypothyroid states and euthyroid goitrous states, including those with primary lack of thyroid tissue or hormone, lack of TSH or TRH and relatively insufficient

hormone with goiter and elevation of TSH. The majority of hypothyroid cases are primary failure due to autoimmune thyroiditis (Hashimoto's).

Symptoms of Hypothyroidism

Complaints include lack of energy, fatiguability, cold intolerance, dry skin, and a tendency to gain weight. Elderly patients may present with any of the above, plus somnolence and lethargy. Females may present with menorrhagia or infertility. Angina is no more frequent than expected in the untreated state, though it may commence with hormone treatment of hypothyroidism. Constipation is a common complaint, caused by sluggish peristalsis. Occasionally, the patient may complain of cold intolerance. Headaches are common, and patients may have syncopal attacks whose prolonged duration may presage the onset of myxedema coma.

The extreme form, myxedema, is more likely to be found in the neglected, isolated, or medically underserved population. These patients may complain of dyspnea due to pleural or pericardial fluid. Myxedema of the hypopharynx contributes to sleep apnea and hypoventilation.

Physical Findings in Hypothyroidism

The hallmarks are cool, dry, puffy skin, particularly about the face, narrowed pulse pressure and bradycardia. The thyroid may or may not be palpable or enlarged, depending on the type of thyroid disease. Pericardial effusion of a proteinaceous and mucopolysaccharide-rich fluid contributes to an enlarged percussible cardiac silhouette. Deep tendon reflexes are characteristically slow and lag in the recovery phase. Agitation and prolonged syncope may precede coma. Dementia in the elderly can be caused by hypothyroidism and often confused with Alzheimer's disease. The dementia clears with treatment of the underlying cause.

It behooves the doctor to recognize hypothyroidism in the newborn, the child, the youth, and the aged. Extreme newborn hypothyroidism is cretinism, which results in irreversible mental and developmental retardation. It must be considered on the basis of nonspecific signs, such as bulging fontanelle, delayed meconium passage, or persistent neonatal jaundice, perhaps telegraphed by hypothyroid appearance and/or the clinical setting.

Laboratory Studies in Hypothyroidism

Table 32.1 lists thyroid function tests. In primary hypothyroidism, the T4 is abnormally low and the TSH elevated. Elevated TSH may occur well in advance of hypometabolism. Hyponatremia, when present, is explained by inappropriate antidiuretic hormone secretion resulting in water retention. Achlorhydria occurs in about *one-half* of patients with primary hypothyroidism; overt pernicious anemia in about 12%. The earliest abnormality

Table 32.1.
Thyroid function tests.

Test	Description and Use
Sensitive TSH (immunoradiometric)	Lower limit of detection, 0.1 μU/mL; test of choice in management of hypothyroidism
Conventional TSH (radioimmunoassay)	Lower limit of detection, 1 μU/mL
Total T ₄	Measures all T ₄ bound to plasma proteins; concentration varies with changes in plasma proteins
Free T ₄ index	Estimate of free T ₄ , calculated by multiplying RT ₃ U by total T ₄ ; corrects for variations in thyroxine-binding globulin
RT ₃ U	Indirect measurement of thyroxine-binding globulin (the main protein that binds T ₄)
Free T ₄ (immunometric techniques)	Influenced by serum levels of lipids, proteins, and certain drugs; some researchers believe it is superior to free T ₄ index
Free T ₄ (equilibrium dialysis)	“Gold standard” of free T ₄ assays
TRH challenge	Measures TSH after thyrotropin-releasing hormone is injected; test has been replaced by the sensitive TSH assay for most purposes
T ₃ radioimmunoassay	Rarely used in management of hypothyroidism
Antithyroid antibodies, antimicrosome antibodies	Neither sensitive nor specific; used to help determine likelihood of autoimmune thyroiditis and conversion from subclinical to overt hypothyroidism

T₃, Triiodothyroinine; T₄, thyroxine; RT₃U, resin T₃ uptake; TRH, thyrotropin-releasing hormone; TSH, thyroid-stimulating hormone.
Rudy DR, Tzgournis M. Endocrinology. In: Rakel RE. Textbook of family practice. 5th ed. Philadelphia: WB Saunders, 1995:1101.

of primary hypothyroidism is TSH elevation. In developing clinical hypothyroidism, TSH elevation may be followed by a phase in which T4 concentration is depressed, but T3 is either normal or even slightly elevated.

Many with primary thyroid disease will never manifest hypometabolism but show only an elevated TSH level, stimulating the gland enough to produce adequate thyroid hormone (5). Some of these eventually manifest nontoxic (euthyroid) goiter. Others, especially the elderly and females, may be classified as subclinical hypothyroidism, defined as TSH = 5 to 20 $\mu\text{U/mL}$ without symptoms, signs and T4 or T3 abnormalities. There is an 8% chance of developing clinical hypothyroidism within 5 years in such cases, and the presence of antimicrosomal antibodies or advanced age increase the risk of overt clinical hypothyroidism.

The total T4 may be elevated in the euthyroid state under the influence of estrogen or pregnancy. The opposite effect occurs with testosterone, glucocorticoids, cirrhosis, and the nephrotic syndrome. The measurement of free T4 avoids such spurious laboratory findings.

If the TSH is not elevated, the presence of decreased T4 and/or T3, pituitary based or trophoprivic hypothyroidism is a possibility. CT scan of the sella tursica allows evaluation of pituitary disease. Assessment of the remainder of the pituitary-endocrine axis is warranted and includes a serum prolactin level, and other pituitary hormone measurements.

Radioactive iodine uptake (^{123}I) is depressed in thyroprivic hypothyroidism. In goitrous hypothyroidism, ^{123}I uptake is normal or even elevated since there is no lack of glandular tissue but rather blockade in hormone manufacture.

Thyroid tests, and in some cases true thyroid function, are influenced by many medications. Their effects on thyroxine binding globulin, TSH, and on true thyroid function are summarized in Table 32.2.

Specific Types of Hypothyroidism

Hyroprivic hypothyroidism. The most common types are postablative hypothyroidism (postradioiodine therapy and surgery) and primary idiopathic hypothyroidism. Others are thyroid aplasia or dysplasia (including sporadic athyreotic cretinism). T4 and T3 levels are abnormally low and TSH elevated.

Table 32.2.**Drugs that affect thyroid function test results.**

Drug	Mechanism
Amiodarone HCl (Cordarone)	Induces hypothyroidism and hyperthyroidism; interferes with T ₄ metabolism
Corticosteroids	Suppress TSH; decrease thyroxine-binding globulin; block conversion of T ₄ to T ₃
Cough medications	Can induce hypothyroidism if preparation contains iodine
Dopamine HCl (Dopastat, Intropin)	Suppresses TSH
Estrogens	Increase thyroxine-binding globulin, falsely increasing total T ₄ level
Lithium (Eskalith, Lithane, Lithobid)	Induces hypothyroidism by blocking secretion of T ₄ and T ₃
Phenytoin sodium (Dilantin)	Interferes with binding of T ₄ to plasma proteins; decreases total T ₄ level; may decrease free T ₄ level
Salicylates	Interfere with binding of T ₄ to plasma proteins when given in high doses; decrease total T ₄ level but not free T ₄ level

T₃, triiodothyronine; T₄, thyroxine; TSH, thyroid-stimulating hormone.

Rudy DR, Tzgournis M. Endocrinology. In: Rakel RE. Textbook of family practice. 5th ed. Philadelphia: WB Saunders, 1995:1101.

Postablative hypothyroidism occurs in 30% of patients after subtotal thyroidectomy, usually within the first year. Therapy may be held in abeyance for a few months since hypothyroidism may occur after surgery and then remit after 1 to 2 months. ¹³¹I therapy for thyrotoxicosis requires much longer for postablative hypothyroidism to emerge, and patients must be treated presumptively or followed for life.

Primary idiopathic hypothyroidism is the second most common type of thyroprivic disease. Females outnumber males, and the disease tends to occur in the 40s- and 50s-age groups. The vast majority manifest antithyroid antibodies.

Endemic goiter (iodine deficiency goiter). The cause is virtually always dietary iodine deficiency, in the past associated with certain geographic areas. Only a minority of the population in endemic areas develop the disease, suggesting that an inherited tendency is required for iodine deficiency to be expressed. Endemic cretinism in these geographic areas occurs only when both parents are effected. The disease in North America has virtually disap-

peared since the advent of iodized salt. Repletion of iodine results in disappearance of the hyperplastic goiter but not the colloid or multinodular goiter.

Goiter due to goitrogenic agents. Drugs in the standard armamentarium that are antithyroid and hence goitrogenic include the antithyroid drugs, lithium, phenylbutazone, topical resorcinol, and the antituberculous drugs, para-aminosalicylic acid and ethionamide.

Thyroid aplasia/dysplasia. Sporadic cretinism (congenital athyreotic cretinism) comprises most of this category. Other cases occur secondary to maternal medication such as iodine-containing preparations or as endemic cretinism.

Trophoprivic hypothyroidism. Postpartum pituitary necrosis (Sheehan syndrome) and periods of hypotension are the most common causes of this syndrome. TSH measurement whenever hypothyroidism is suspected allows differentiation of this disease from primary hypothyroidism. This is critical to avoid precipitation of adrenal insufficiency by treating hypothyroidism without treating the underlying pituitary insufficiency.

Management of Hypothyroidism

Levothyroxine (Levoxine, Synthroid) has a half-life of about 8 days, similar to that of thyroxine (tetraiodothyronine, T₄), requiring about 4 weeks for full effect and about that long to abate. It is metabolized to T₃ and T₄. Tablet sizes are multiple and allow precise dosing. The adult requires full replacement 1.7 $\mu\text{g}/\text{kg}/\text{day}$ (ideal body weight) or 120 μg (0.12mg) for the average-sized person. Children may require dosages up to 4 $\mu\text{g}/\text{kg}/\text{day}$, while elderly adults require less than 1 $\mu\text{g}/\text{kg}/\text{day}$. Patients older than 50 years or younger patients with heart disease should be started on low dosages (0.025) and graduated upward in intervals of 6 to 8 weeks until TSH levels are normal. For optimal absorption levothyroxine should be administered 4 hours apart from doses of cholestyramine, ferrous sulfate, sucralfate, or aluminum hydroxide containing antacids. Phenytoin, carbamazepine, and rifampin accelerate metabolism of levothyroxine, which may necessitate higher dosages.

Tri-iodothyronine (liothyronine), a synthetic drug with a "short" half-life (Cytomel, Triostat, Thyrar), is suited to situations in which it may be unsafe to commit the patient to a long-acting preparation impossible to withdraw quickly, e.g., at the first sign

of angina, coronary disease, or myxedema heart disease. Liothyronine is used for maintenance only in unusual circumstances such as adverse reactions to levothyroxine. The average replacement dosage is 75 to 100 μg daily. The required dosage may increase with treatment and as the thyroid hormones are cleared more rapidly. Therefore, TSH should be remeasured several months after apparent achievement of the euthyroid state.

Rapid treatment is necessary only in myxedema or severe hypothyroidism with acute infection to avoid the supervention of sepsis. Liothyronine may be dosed at 25 μg each 8 hours or 500 μg of levothyroxine may be given intravenously.

In cretinism of the newborn rapid correction of T4 to 10 $\mu\text{g}/\text{dL}$ (130 nmol/L) is necessary, and the level must be maintained for the first 4 years in order to avoid permanent mental retardation and indefinitely to treat the ongoing state of hypothyroidism. The usual starting dosage is 50 μg of T4.

Nontoxic Goiter (Euthyroid Goiter, Simple Goiter). These are an aggregation of disorders with multiple causes of inefficient hormone production. Some are hypothyroid goiter, and would include iodine deficiency and those caused by antithyroid agents; others are characterized by defective hormone synthesis. Nontoxic goiters occur more frequently in females as compared with males (8:1). Hyperplasia in response to TSH stimulation occurs usually as a result of intermittent lack of hormone. The goiter, usually diffuse, regresses when TSH is suppressed by thyroid hormone.

Some hyperplastic areas develop into hormone-producing nodules after variable periods of time. Most still respond to TSH but some become autonomous. Patients are likely to be over 50 years old and may have had undetected diffuse goiters for long periods of time. Outcomes possible at this stage include euthyroid and hypothyroid nodular goiter, hyperplastic nodule, and toxic nodular goiter.

Physical examination reveals a palpable enlarged gland that may resemble a nodular goiter or that of Grave's disease. Diffuse goiter may be confused with Hashimoto's thyroiditis, which can be differentiated by the presence of antithyroid antibodies.

Laboratory Findings in Nontoxic Goiter. Serum T3 and T4 concentrations are normal. ^{123}I uptake is normal or slightly elevated. TSH may be mildly elevated in the young person with simple diffuse goiter but is usually normal in nontoxic nodular goiter.

Treatment of Euthyroid Goiter. The goal is not only reduction of gland size and early prevention of hypothyroidism but also prevention of overstimulation by TSH and possible toxic multinodular goiter. Thyroid therapy alone (0.1 to 0.15 mg daily) effects reduction of TSH to normal and regression of the goiter, usually less than completely. In *nontoxic nodular goiter*, suppression is not always successful, but is propitious if the TSH level is greater than 0.5 mU/L. Follow-up of the thyroid tests and goiter size is appropriate. If the T4 level increases and TSH is suppressed, there may be autonomy in single or multiple nodules. ^{131}I is the treatment of choice for those goiters that develop autonomously secreting nodules resulting in hyperthyroidism.

THYROIDITIS

The following categorization facilitates differentiation of this group of conditions clinically and pathologically:

Acute thyroiditis is a rare condition reflecting an infection of the thyroid, most often found in women ages 20 to 40. As the thyroid is normally resistant to infection, this entity occurs in abnormal glands such as nodular goiter (50%), thyroglossal duct remnants, internal fistulae, or immune-compromised individuals. The symptoms and signs are those of suppurative disease; hypermetabolism usually does not occur. Treatment is surgical drainage as needed and antibiotics.

Subacute thyroiditis occurs in two forms sometimes called "painful" and "painless." Viral disease often has an acute and painful course, sometimes reminiscent of "acute thyroiditis." Synonyms are *granulomatous thyroiditis*, *painful thyroiditis* and *De Quervain's thyroiditis* and has been associated with many viruses, including mumps. Two-thirds of Caucasian and Chinese patients share the HLA type Bw-35. Eighty percent of cases are women (6). Hypermetabolism occurs in 50% of cases of subacute granulomatous thyroiditis, due to released T4 more than T3. ^{123}I uptake is depressed during the acute phase due to a fault of iodine incorporation. The sedimentation rate is always elevated, usually above 50 mm/hour. Symptoms last 2 to 4 weeks subacutely and up to 6 months ultimately. Two and one-half percent have residual goiter; 5% develop hypothyroidism, more likely in those who had transient phases of hypermetabolism. The treatment is salicylates, other nonsteroidal medications, and occasionally glucocorticoids.

Painless thyroiditis occurs postpartum usually, but a few cases are sporadic. Postpartum painless thyroiditis manifests an 80% prevalence of autoimmune microsomal antibodies. Thyrotoxicosis as a presentation of painless thyroiditis accounts for a significant proportion of the *incidence* of thyrotoxicosis (6). Severe cases are likely to progress through the stages that lead to hypothyroidism. Goiter is present in up to 48%, and recurrent hyperthyroidism occurs in 11%. As with other thyroiditides, this entity is differentiated from Grave's disease by the finding of depressed radioiodine uptake in the face of hypermetabolism, as well as the absence of TSH receptor antibodies. Treatment with beta-adrenergic blocking agents works well to control the hypermetabolic phase. Thyroid hormone replacement is necessary if hypothyroidism occurs.

Chronic Thyroiditis

Hashimoto's disease (struma lymphomatosa) is a common disease with an autoimmune cause. It occurs in subclinical variants, and can be detected by the presence of autoantibodies. TSH activity, increased in response to a defect in hormone synthesis, produces glandular hyperplasia as in other goiter formation. Mostly thyroglobulin and microsomal antibodies are involved. Associations with HLA B-8, DR-3,4, and 5 are evidence of a genetic predisposition. Environmental assaults that may precipitate the disease include viral and bacterial infection (*Yersinia enterocolitica*) and excessive iodine. Ninety-five percent of patients are middle-aged women. Five percent of cases present with hyperthyroidism and 20% with hypothyroidism, but most present with asymptomatic goiter.

Radioactive iodine uptake might be elevated as a result of the aberrant TSH effect of the antithyroglobulin antibodies, though the patient might be euthyroid. The foregoing notwithstanding, TSH itself is elevated due to incipient hypothyroidism, based in turn on impaired hormone manufacture. There is usually a diffusely palpable, firm goiter, but on occasion, a single palpable lobe or nodule. End-stage Hashimoto's thyroiditis thus accounts for the highest proportion of thyroprivic primary hypothyroidism. On rare occasions, Grave's disease may emerge from this pathophysiology. Euthyroid or hypothyroid patients require TSH suppression by thyroid hormone to arrest the growth of the goiter, and to reduce the gland size to normal. A typical regimen is levothyroxine 1.7 μ g/kg daily for adult patients (0.1 to 0.15 mg).

Riedel's thyroiditis (Riedel's struma), "woody thyroid", is a rare chronic thyroiditis characterized by a gland of hard consistency, affecting women:men 3:1, felt to be one of a group of syndromes of multifocal idiopathic fibrosis. The total grouping is called the idiopathic inflammatory fibrosclerosing syndromes, and can involve retroperitoneal and mediastinal spaces and the cervix and may produce cholangitis and orbital pseudotumor. Its name characterizes the hard consistency of the goiter, which may involve either or both lobes and produce mechanical interference with swallowing and breathing. The patient may be euthyroid or hypothyroid. Surgery is the only specific treatment, for relief of mechanical problems. Otherwise, the TSH should be followed for detection of hypothyroidism. Rarely, the disease may be progressive and even fatal.

SICK EUTHYROID SYNDROME

This is a term given for the combination of abnormalities involving the transport, metabolism, and regulation of thyroid hormones in various states of illness. The significance of these effects is realized by the statistic that while 70% of hospitalized patients may have a depressed T3, only 1% have unsuspected hypothyroidism. T4, free T4 and free T4 index may be normal or increased in mild illness and depressed in patients with critical illness (7). Despite the low T4 and T3 levels, TSH levels tend to be low and the TRH responses are blunted.

THYROID NEOPLASMS

Benign

This discussion does not include the goiters already addressed. Microfollicular adenoma, macrofollicular adenoma, embryonal adenoma, fetal adenoma, and Hürtle cell adenoma may present as solitary nodules. In the course of evaluation, their identity becomes known as a result of histopathological examination.

Malignant

Carcinoma of the thyroid comprises about 1% of the cancer incidence in the United States, carries a case fatality rate of about 10%, and causes 1000 deaths per year. Thyroid cancer is estimated to have a 10,000 to 14,000 incidence in the United States

(8). Seventy-seven percent of the incidence, but only 61% of the mortality is in females, because the prognosis in males is worse with papillary carcinoma. Table 32.3 lists the properties and distinguishing characteristics of the thyroid carcinomas.

Papillary carcinoma accounts for 75% of all thyroid carcinomas. Females are affected 3:1 over males. The tumor affects mainly people from young adulthood through the 50s, with the worst prognosis in the 50s. Childhood irradiation to the neck area confers a 5% risk of developing this tumor and a four-fold increase in adenoma. Though regional node metastasis is present in 30% to 50% at the time of presentation, only 5% to 7% metastasize beyond the adjacent lymphatics. The prognosis is >95% survival for ≥20 years. The cancer is multicentric and is commonly found incidentally as occult foci, by definition less than 5 mm in diameter or as incidental nodule(s) in an asymptomatic euthyroid. The nodule is “cold” on ¹²³I uptake. Variants of papillary carcinoma include *columnar cell*, *diffuse sclerosis*, and *encapsulated papillary carcinoma*.

Follicular carcinoma. This variant appears to arise from papillary carcinoma and makes up 16% of all thyroid cancers. Patients are older on average. While regional lymph node spread is less likely, hematogenous spread is more so; thus, there is greater likelihood for distant metastases and a poorer prognosis. Survival varies from 44% to 86%, inversely with the aggressiveness of the cell type. Older patients have the worse prognosis. While follicular carcinoma is a relatively “cold” nodule on RAI uptake, it manifests some TSH responsiveness and takes up some iodine.

Table 32.3.
Properties and characteristics of thyroid neoplasms.

Neoplasm	Proportion (%)	Gender Prevalence	Age Range (years)	Prognosis
Papillary Ca	50–80	3:1 F > M	20–60	90% at 20 years
Follicular Ca	10–15	3:1 F > M	40–60	44–80% at 10 years (< aged)
Anaplastic Ca	10	F ≥ M	>50	Poor (months)
Medullary Ca	2–10	F ≥ M	>40	67% to 10 years ^a

^aEighty percent of medullary carcinomas occur in sporadic form, 20 percent are familial, including MEN-2A and MEN-2B.
Rudy DR, Tzgournis M. Endocrinology. In: Rakel RE. Textbook of family practice. 5th ed. Philadelphia: WB Saunders, 1995:1104.

Treatment of papillary and follicular carcinomas is total thyroidectomy or subtotal thyroidectomy followed by an ablative dose of ^{131}I . Metastatic lesions responsive to TSH are amenable to therapeutic ^{131}I , e.g., 100 to 150 mCi. Levothyroxine suppression of TSH is carried out indefinitely.

Anaplastic. These cancers comprise 3% of all thyroid tumors. Many show histologic evidence of papillary origin, possibly the result of metamorphosis from pre-existing adenomatous goiters. They are very aggressive and carry a poor prognosis. Treatment consists of palliative surgery and irradiation (9).

Medullary carcinoma. This tumor comprises 5% of all thyroid cancers. It may be a part of multiple endocrine neoplasia (MEN). In MEN 2-A, it is associated with pheochromocytoma and hyperparathyroidism, and in MEN 2-B, with marfanoid habitus, neuromas and/or pheochromocytoma. It may occur separately as an autosomal dominant familial tumor or sporadically. It elaborates calcitonin, which also serves as a tumor marker. In addition it may produce 5-hydroxytryptamine, adrenocorticotrophin, somatostatin, prostaglandins, and carcinoembryonic antigen (CEA). Patients present with symptoms of growing space occupying goiter. Treatment is total thyroidectomy. Patients and their relatives should be screened for MEN 2-A and 2-B.

Lymphoma rarely develops in the thyroid and tends to be associated with Hashimoto's thyroiditis, roughly a 0.5 % risk.

EVALUATION OF THE SOLITARY THYROID NODULE

First, it must be recognized that 4% to 7% of the population have palpable nodules of the thyroid and up to half have nodules detectable by ultrasound or autopsy (10). A dominant nodule within a multinodular gland is as much of a concern as a solitary nodule. Only 5% to 10% of palpable nodules will be cancerous. Suspicion should arise with thyroid nodules in men over 60 years of age, those that are fixed, stony hard, those with associated lymphadenopathy, and those in glands exposed to radiation.

Patients with elevated TSH levels can be assumed to have clinical or incipient hypothyroidism, treated empirically with thyroid hormone for 3 to 6 months and re-evaluated after TSH has returned to normal. Metabolism may be corroborated by free or total thyroxine measurements. Those patients with a nodule and suppressed TSH should be further tested to determine if thyrotoxicosis is present. A hyperfunctioning solitary nodule con-

firmed by ^{123}I uptake and scan is treated as a benign, toxic adenoma. However, 4% of those with TSH suppression (0.4% of the total) may be malignant. Thus, they must be followed while on therapy and re-evaluated if needed.

In the past, fine needle aspiration biopsy (FNAB) was done on all patients with "cold" nodules on ^{123}I uptake/scan. This has been challenged on the basis that 90% to 95% of all cold nodules are benign, a rate comparable with all nodules (10). Those with normal TSH measurements comprise the majority.

The following are the preponderant diagnoses of clinically solitary nodules: adenoma [follicular (colloid, microfollicular, embryonal, Hürtle cell)], approximately 74%; carcinoma, 4% (papillary, 70%, follicular, 15%, medullary, 5% to 10%, anaplastic, 5% and lymphoma, 5%), cyst, nodule of a multinodular goiter (10); and the remainder indeterminate. At the Mayo Clinic sensitivity of FNAB was shown to be 93.5%, specificity 87%. Malignant findings are more likely to occur in males than in females; young patients (under 30) and older patients (increasingly with age as it progresses above 60 years) (11).

THE SOLITARY NODULE

From a different vantage point, patients with nodular thyroid disease may be categorized as follows, by increasing risk of malignant tumor as modified from Haugen (10):

Low risk: Female sex without stony or fixed nodule

Proportion of cases: 44%

Malignancy: 11%

Moderate risk: Age <20 years or >60 years, male sex, history of neck irradiation, size >4 cm, fixation questionable

Proportion of cases: 38%

Malignancy: 14%

High risk: Growth rapid, firm nodule with fixation, vocal cord paralysis or enlarged lymph nodes

Proportion of cases: 18%

Malignancy: 71%

Indeterminate results, defined as insufficient tissue, histologically normal tissue in the presence of a definite nodule, are ap-

proached by repeated biopsies. Ultrasound is of greatest help in following nodularity during suppression.

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Triage of Problems of the Adrenal Gland

Vidya Sundaram and James M. Falko

RECOGNITION OF PROBLEMS OF ADRENALS

Adrenal disorders should be suspected in patients presenting with a combination of symptoms of fatigue, alterations in blood pressure, weight gain/loss, electrolyte imbalance, especially hyponatremia and hyperkalemia, menstrual disorders, skin pigmentation, or hirsutism.

Adrenal Insufficiency

Primary adrenal insufficiency is rare and is due to intrinsic disease of the adrenals secondary to autoimmune atrophy, bilateral adrenal hemorrhage, fungal infections, tuberculosis, AIDS, or metastatic cancer to the adrenals such as breast or lung cancer.

Secondary adrenal insufficiency is more common, usually due to suppression of the hypothalamic-pituitary-adrenal (HPA) axis due to exogenous corticosteroid therapy, but may also be due to any lesion in the hypothalamus or the pituitary gland.

Diagnosis

Rapid ACTH stimulation test (cosyntropin [Cortrosyn] test) can be done as an outpatient, any time of the day, and is an appropriate screening test.

Procedure. Obtain baseline serum cortisol, ACTH and aldosterone levels. Inject 250 µg of cortrosyn intramuscularly or intravenously

and repeat samples for cortisol and aldosterone at 30 and 60 minutes.

Results	Normal	Primary Adrenal Insufficiency	Secondary Adrenal Insufficiency
Peak cortisol post Cortrosyn	>20 $\mu\text{g/dL}$	<20 $\mu\text{g/dL}$	<20 $\mu\text{g/dL}$
Peak aldosterone post Cortrosyn	>16 $\mu\text{g/dL}$	<16 $\mu\text{g/dL}$	>16 $\mu\text{g/dL}$
Baseline ACTH	NI	High	Low or NI

Note that a cortisol level of at least 20 $\mu\text{g/dL}$ usually excludes any element of adrenal insufficiency.

Other tests of ACTH secretory reserve to diagnose secondary adrenal insufficiency are usually done in consultation with an endocrinologist.

Treatment

Maintenance Therapy. Usual daily *glucocorticoid* replacement dosage is prednisone 5 mg every AM and 2.5 mg every PM or hydrocortisone 20 mg every AM and 10 mg every PM. Higher dosages may be required if patient is extremely obese or active, or patient takes drugs known to induce hepatic metabolism, e.g., barbiturates, rifampin, phenytoin.

Patients with primary adrenal insufficiency also need *mineralocorticoid* replacement with fludrocortisone (Florinef), usually 0.05 mg to 0.1 mg per day as a single daily dose. The dose is increased if patient has hyperkalemia or orthostatic hypotension and decreased if hypertension, edema or hypokalemia is present.

Perioperative Management. For procedures requiring general anesthesia: On the day of surgery: 100 mg hydrocortisone intravenously at 7:00 AM or 1 hour prior to the procedure and subsequently 100 mg intravenously every 8 hours until the patient's condition is stable postoperatively. The dosage of hydrocortisone is then tapered by 30% to 50% each day over the next 3 to 5 days.

Hydrocortisone is preferred in primary adrenal insufficiency because it also has mineralocorticoid activity, and there is no need to add fludrocortisone. However, in patients receiving oral glucocorticoids for anti-inflammatory or immunosuppressive purposes, methylprednisolone (which has little or no mineralocorticoid activity) can be used instead.

Glucorticoid Coverage During Stress. For *minor illnesses* (e.g., colds, diarrhea), or minor surgical procedures under local anesthesia or routine dental work: double the maintenance dosages. If nausea or vomiting precludes oral intake then give glucocorticoids parenterally. Patients should be educated to adjust the dosage in minor illnesses and should wear a Medic-Alert bracelet indicating their steroid dependency. For *major stress*, e.g., trauma, sepsis: the equivalent of 200 to 300 mg of hydrocortisone per day.

Adrenal Hyperfunction

Cushing’s Syndrome and Disease

Cushing’s syndrome occurs as a result of excess secretion of steroids from the adrenal cortex (endogenous) or as a result of sustained administration of exogenous glucocorticoids.

Endogenous Cushing’s Syndrome. Pituitary Cushing’s syndrome (Cushing’s disease): due to pituitary microadenoma or macroadenoma producing excess ACTH.

Adrenal Cushing’s syndrome: secondary to adenoma, carcinoma or micronodular hyperplasia secreting excess cortisol.

Ectopic Cushing’s syndrome: secondary to ectopic production of ACTH , usually bronchial carcinoids.

Clinical Presentation. Common findings are central obesity with supraclavicular fat pads, phlethoric facies, hypertension, glucose intolerance, easy bruising, purple striae, proximal muscle weakness, menstrual dysfunction, hirsuitism, osteoporosis, or depression.

Screening Tests.

Overnight 1 mg dexamethasone suppression test:

Dexamethasone 1 mg is given at 11 PM and plasma cortisol is obtained at 8 AM. False positives: in depression, alcoholics, obesity, patients on estrogens, drugs that accelerate hepatic metabolism like dilantin, barbiturates, rifampin.

24-hour urine free cortisol:

Tests	Normal	Cushing’s syndrome
24-hour urine free cortisol	Normal	↑ (>250 µg is diagnostic)
Overnight 1 mg dexamethasone suppression test	8 AM cortisol < 5 µg/dL	>10 µg/dL

Note that the 24-hour urinary free cortisol is not affected by estrogens.

Endocrine referral is appropriate if there is clinical suspicion and the screening tests are suggestive of Cushing's syndrome.

Further diagnostic studies after positive screen:

Tests	Pituitary Cushing's disease	Adrenal Cushing's syndrome	Ectopic Cushing's syndrome
8 mg overnight dexamethasone suppression test	24-hour urine 17 OHCS* and plasma 17 OHCS ↓ by >50%	usually does not suppress	usually does not suppress
Plasma ACTH	↓ or N	↓↓	↑↑

*17 OHCS = 17 hydroxy corticosteroids

Other tests to differentiate the source of Cushing's syndrome include: a) CRH stimulation test, b) Inferior petrosal sinus sampling. These are usually done in consultation with an endocrinologist.

Localization Procedures.

MRI of the pituitary gland.

CAT scan of adrenal glands and lungs.

Inferior petrosal sinus sampling.

Treatment

Pituitary Cushing's syndrome. Optimal treatment is transsphenoidal resection of pituitary adenoma. External irradiation in doses of 4500 to 5000 Gy if surgery fails to cure. Medical therapy with adrenal enzyme inhibitors such as ketoconazole to control symptoms prior to surgery or chronic control of hypercortisolism. Other drugs that can be used are mitotane, metyrapone, aminoglutethemide.

Adrenal Cushing's syndrome. Surgery is the treatment of choice; unilateral adrenalectomy in case of adenomas and bilateral adrenalectomy in case of micronodular hyperplasia or carcinoma. Additional therapy with mitotane may be needed for adrenal carcinoma.

Ectopic Cushing's syndrome. Surgical removal of ACTH-secreting tumor is the treatment of choice. If that is not feasible, bilat-

eral adrenalectomy or medical therapy with adrenal enzyme inhibitors may be considered.

Primary Hyperaldosteronism

Primary hyperaldosteronism is an uncommon adrenal cause of hypertension seen in 1% to 2% of hypertensive patients. The most common causes are aldosterone-producing adrenal adenoma (60%), idiopathic hyperaldosteronism with bilateral micronodular hyperplasia of the adrenals (40%).

Clinical Presentation. Hypertension is always present and may be quite severe. Significant hypokalemia <3.5 mEq/L and symptoms related to it, e.g., polyuria, polydipsia, fatigue, muscle weakness, cramping, and, in severe cases, paralysis. Mild metabolic alkalosis; correlates to degree of hypokalemia. Physical examination is not helpful; edema is usually absent.

Screening Tests.

Serum and Urinary Potassium. Severe unprovoked hypokalemia of ≤ 2.7 mEq/L and urinary potassium greater than 30 mEq/24 hours in face of hypokalemia is due to primary hyperaldosteronism in the great majority of the cases. It is unusual for diuretics to lower serum potassium levels to <3 mEq/L. Measurements should be repeated after diuretic therapy has been discontinued.

Plasma Renin Activity (PRA), Plasma Aldosterone. PRA is usually low or suppressed and aldosterone levels are usually high in primary hyperaldosteronism.

Drugs that affect the renin-angiotensin-aldosterone system like ACE inhibitors, diuretics, beta blockers, calcium channel antagonists, and spironolactone interfere with determination of the ratio and should be discontinued 2 to 3 weeks prior to obtaining levels of aldosterone and PRA. The patient should also have adequate salt intake and potassium replacement.

Plasma Aldosterone (ng/dL) to PRA (ng/mL per hour) Ratio. A ratio greater than 20 has a 100% sensitivity and 75% to 80% specificity in identifying patients with this disorder.

24-Hour Urine for Aldosterone. A value greater than $12 \mu\text{g}$ /24 hours along with a suppressed PRA provides strong evidence for diagnosis.

Saline Suppression Test. Administering 2 L of 0.9% saline intra-

venously over 4 hours will suppress plasma aldosterone by at least 50%, or to less than 5 ng/dL in normal individuals but will not suppress in primary hyperaldosteronism.

Endocrine Referral. This is appropriate for patients without: unexplained hypokalemia; evidence for hyperaldosteronism on screening tests.

Treatment. For adenomas, hypertension resolves in 80% of patients following surgery. Medical management is invoked for patients with idiopathic hyperaldosteronism or patients who are not fit for surgery. This consists of spironolactone 100 to 200 mg/day. Additional antihypertensive therapy with calcium channel blockers or ACE inhibitors may be required.

Pheochromocytoma

Pheochromocytoma is a rare catecholamine secreting tumor of the sympathoadrenal system that is found in approximately 0.1% of hypertensive patients.

Clinical Presentation. Patients have frequent episodes of paroxysmal symptoms of headache, palpitations, flushing, nervousness, sweating, chest or abdominal pain, nausea and vomiting. Symptoms may be precipitated by exercise, sexual intercourse, straining, micturition, or ingestion of food or alcohol. Surgical procedures may initiate the attacks. Certain drugs, e.g., beta blockers, hydralazine, guanethidine and ganglionic blockers, cause paradoxical rise in blood pressure. Tricyclic antidepressants, phenothiazines, morphine, and meperidine may also precipitate attacks.

Patients may also present with the complications of severe hypertension, e.g., myocardial infarction, congestive heart failure, stroke, azotemia, dissecting aneurysm. Common physical findings are those of sustained or paroxysmal hypertension, and possibly orthostatic changes in blood pressure. Patients are usually lean, appear anxious and a mass rarely may be palpated in the neck or abdomen. Fundus examination usually shows evidence of grade 1 or 2 hypertensive retinopathy.

Associated Syndromes. Multiple endocrine neoplasia (MEN) types II A and II B; neurofibromatosis; von Hippel-Lindau disease.

Screening. Screening for pheochromocytoma is indicated in the following situations:

1. Hypertension resistant to therapy, all hypertensive children, patients who show a paradoxical rise in blood pressure when treated with beta blockers, hydralazine.
2. Patients diagnosed with MEN IIA or IIB and all their first-degree relatives, even if asymptomatic.
3. Hypertensive episodes during surgery, labor, or radiologic procedures.
4. Radiologic evidence of a suprarenal mass.
5. Needle biopsies of suprarenal masses should not be undertaken prior to urine or plasma screening for pheochromocytoma because of the *risk of producing a severe paroxysmal attack*.

Diagnosis. Tests should be done ideally in a nonstressed environment, and the patient should not be on any drugs or foods that would interfere with the test.

24-Hour Urine Specimen for VMA, Metanephrines, and Free Catecholamines. This is useful for screening, especially if collected following an attack. Seventy-five percent of patients will have total urinary metanephrines greater than 1000 $\mu\text{g}/24$ hours. The vast majority will have total urinary catecholamines (norepinephrine and epinephrine) greater than 150 $\mu\text{g}/24$ hours. If both measurements exceed those limits, chances are 95% that pheochromocytoma is present. Urinary VMA (vanillyl mandelic acid) is the least reliable test due to high incidence of false positives and negatives. Many drugs and foods also interfere with the assay.

Plasma Catecholamines. This sample is collected through an indwelling catheter and after the patient rests supine for 30 minutes. Plasma norepinephrine greater than 2000 pg/mL is highly specific and sensitive for diagnosis.

Clonidine Suppression Test. This test helps to distinguish patients with pheochromocytoma from those with exaggerated physiologic elevations of catecholamine levels. Blood samples for plasma catecholamines are collected at baseline, 2 and 3 hours after administration of 0.3 mg of clonidine. Normal patients suppress their catecholamines to within the normal range at 3 hours while patients with pheochromocytoma do not suppress. Heart rate and blood pressure should be monitored q 30 min during the test.

Tumor Localization. The computed axial tomography (CT) scan is highly reliable in identifying pheochromocytomas in adrenal and extraadrenal locations in 95% of cases. Magnetic resonance imaging (MRI) is also useful. A characteristic signal intensity is seen on T2-weighted images.

The metaiodine-131-iodobenzylguanidine (MIBG) scan is also very sensitive and specific in localizing adrenal and extraadrenal tumors.

Treatment. Treatment is surgical removal of tumor, but the patient needs to be stabilized preoperatively. Seventy-five percent of patients become normotensive after removal of tumor.

Preoperative Management. Acutely, control of severe hypertension is accomplished with alpha blocking agents like intravenous phentolamine or sodium nitroprusside and intravenous hydration in an intensive care setting. Beta blockers are used to control dysrhythmias after adequate alpha blockade has been achieved.

Situations requiring prolonged medical treatment occur in patients with recent myocardial infarction, cardiomyopathy, last trimester of pregnancy, or metastatic pheochromocytoma. Patients are treated with phenoxybenzamine or prazosin, orally. Calcium channel blockers may also be used. Metyrosine, an inhibitor of tyrosine hydroxylase, is used in inoperable cases or in patients with malignant pheochromocytoma.

Endocrine referral is appropriate for patients with severe hypertension resistant to treatment; patients with elevated urine or plasma catecholamines, or evidence of a pheochromocytoma; a positive family history for familial syndromes like MEN; or patients who have radiologic evidence of a suprarenal mass.

Congenital Adrenal Hyperplasia (CAH)

CAH is a family of disorders caused by deficient activity of one of the enzymes involved in cortisol synthesis. The important disorders are 21-hydroxylase deficiency (most common); 3 β -hydroxysteroid dehydrogenase deficiency (rare); 11-hydroxylase deficiency (rare); 17-hydroxylase deficiency (rare).

Clinical Presentation. Usually the classic forms of the disease present in infancy as salt wasting crises, ambiguous genitalia, virilization, or sexual infantilism. However, the late-onset or nonclassic

forms present with hyperandrogenism after puberty, i.e., hirsutism, menstrual disorders (amenorrhea, oligomenorrhea), infertility, acne, and/or temporal balding in women.

Screening Tests.

Disorder	21-hydroxylase deficiency	3β-hydroxy-steroid dehydrogenase deficiency	11-hydroxylase deficiency	17-hydroxylase deficiency
Lab findings	↑17 OH progesterone	↑17 OH pregnenolone and DHEA	↑11-deoxy cortisol and deoxy-corticosterone costerone	↓17 alpha hydroxy steroids
1 hr. post ACTH stimulation test	↑↑↑17(OH) progesterone	↑↑17 OH pregnenolone and DHEA	↑↑levels of 11-deoxy cortisol and deoxy corti-costerone	poor response to ACTH

Endocrine referral may be considered in patients with symptoms of hyperandrogenism, ambiguous genitalia, abnormal growth, premature pubarche, abnormal tests, as mentioned above, or pregnancy.

Treatment and Follow-up. Treatment, in classic forms, consists of replacement of deficient steroid hormones, i.e., glucocorticoid and mineralocorticoid therapy, and increased salt intake. In the non-classic forms a small dose of dexamethasone (0.25 to 0.5 mg) or an equivalent dose of prednisone at bedtime usually suppresses the androgen production. Patients need to be monitored for side effects of glucocorticoid therapy. Prenatal diagnosis of CAH is important in women who have a positive family history because treatment is necessary to avoid ambiguous genitalia in a female fetus.

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Problems of Growth and Development

Dara P. Schuster and James M. Falko

Appropriate growth and development provide a window into the child's overall health and well-being. Growth is defined as the increase in size and development as an increase of complexity (1). Growth is determined by both genetic factors and the environment (1, 2, 3).

Normal growth velocity varies with age: 1–6-month growth velocity is 18–22 cm/yr; 6–12-month, 14–18 cm/yr; 2nd yr, 11 cm/yr; 3rd yr, 8 cm/yr; 4th yr, 7 cm/yr; 5–10 yr, 5–6 cm/yr (4). The minimal growth velocity after infancy is considered to be 5 cm/year (2 inches/year). Growth tends to occur in spurts rather than progressing at a continuous rate (1). Because of this, it is important to establish the pattern of growth for an individual child and to determine growth velocity. The presence of height acceleration or deceleration is an important indicator for some disease processes.

The upper-to-lower (U/L) segment body ratio changes with growth of the child. The lower body length (pubis to sole) is subtracted from the height to get the upper segment (crown to pubis). At birth, the U/L ratio approximates 1.7:1; by age 8 to 10 the ratio has changed to 1:1, reflecting the growth of the long bones. The normal adult ratio is closer to 0.9. The U/L ratio is affected by certain growth disorders. Chondrodystrophic syndromes have characteristic short limbs relative to the upper body segment (increased U/L ratio). Hypogonadal individuals have increased limb length compared with their upper body segment (eunuchoid proportions or decreased U/L ratio).

When examining growth in children it is important to determine their genetic potentials for height attainment. These can be approximated in the following manner for individuals: First adjust the height of the opposite sex parent by adding 13 cm to mother's height (for boy) or subtracting 13 cm from father's height (for girl), then taking the height of the same sex parent, and averaging the two figures to find the midparental height. Add 8.5 cm above and subtract 8.5 cm below the midparental height to approximate the 3rd to 97th percentile range. This calculation provides a range of height within which the child's projected adult height should fall (5). The projected adult height as a percentile among peers can then be compared with the child's present height and percentile to the child's age/sex peers on the standard growth chart (see Fig. 42.1). If the projected adult height is roughly in the 25th percentile (two-thirds of the span from the 3rd percentile to the midparental height) and the child's height is roughly the 25th percentile for his/her age/sex, the child's height is as expected.

The pattern of growth can provide insight into the cause and temporal nature of the growth abnormality. The discordance of chronological age and skeletal maturation may also provide information on the cause of the growth problem. Skeletal maturation advances inappropriately with exposure to exogenous and endogenous androgens and estrogens. Skeletal maturation may be delayed in constitutional growth delay, growth hormone deficiency, and hypothyroidism. The bone age is assigned based on the skeletal maturation of the wrist and hand. This age is then compared with the child's chronological age to determine if significant advancement or delay in skeletal maturation is present.

DISORDERS OF GROWTH

Growth Deficiency

The definition of short stature requiring medical attention is height that is below the 3rd percentile or 2 SD below the mean height for age/sex. Eighty percent of children more than 2 SD below and 50% of children at more than 3 SD below the mean height for age are normal and have no pathological problems (3).

The causes of short stature are varied and generally can be divided into 7 major areas (2–4).

1. *Constitutional growth* delay represents a slowing in the pace of height attainment. These children are normal in size at birth,

over the first 2 to 3 years have slowing in the growth velocity, resulting in moving to lower growth curves, and then slow steady growth through the completion of puberty, which is typically delayed. This pattern is characterized by family history of a similar pattern of growth and puberty, normal nutritional status and physical examination, heights at or below 3rd percentile for age and normal annual growth rate, delayed puberty, retarded bone age, normal predicted adult height in context of family pattern, no organic or emotional cause for growth failure.

2. *Familial short stature* is characterized by family history of short stature, normal bone age, normal growth velocity, and normal pubertal development.
3. *Chromosomal disorders* resulting in short stature may involve the autosomes such as trisomy 21, Prader-Willi syndrome, or the sex chromosomes as seen in Turner's syndrome.
4. *Cartilage and bone dysplasias* are a heterogeneous group of disorders that include achondroplasia and epiphyseal dysplasia. Often this group of individuals will demonstrate an increased U/L ratio.
5. *Endocrine abnormalities* causing short stature include poorly controlled diseases such as diabetes mellitus, Cushing's syndrome, and vitamin D-resistant rickets and hormone deficiencies such as hypopituitarism, isolated growth hormone deficiency, hypothyroidism, and hypocortisolism.
6. *Nonendocrine illnesses and conditions* frequently cause poor growth. Renal tubular acidosis and chronic inflammatory processes such as juvenile rheumatoid arthritis and inflammatory bowel disease result in a poor environment for tissue growth. Central nervous system problems such as mental retardation and neuromuscular disease are also associated with decreased growth.
7. *Psychosocial short stature*, also referred to as emotional deprivation, maternal deprivation, hyposomatotropism and abuse dwarfism, may result in short stature either by growth hormone suppression associated with extreme degrees of emotional neglect or by physical and nutritional neglect. In most cases, the secretion of growth hormone returns to normal once the child is removed from the adverse environment.

Baseline Screening Studies for Assessment of Short Stature

These include:

- Detailed history and physical examination.
- Analysis of growth pattern from all available data.
- Urinalysis to examine the ability of the kidney to acidify and concentrate urine.
- Chemistry profile (electrolytes, Ca, phosphates, hepatic and renal function), T₄, TSH, ESR.
- Bone age.
- Karyotype to rule out Turner's syndrome if female.
- MRI of the pituitary and hypothalamus to detect abnormality.

If the above work-up is normal, it is reasonable to evaluate possible growth hormone deficiency. Otherwise, abnormalities must be corrected before further testing since many metabolic derangements will result in growth hormone suppression.

Tests to Evaluate Growth Hormone Deficiency

Growth Hormone Stimulation Tests. These include arginine, insulin, clonidine, and L-dopa. It is standard to perform two of the above stimulation tests. Growth hormone deficiency is defined as failure to mount a growth hormone (GH) response of >10 ng/mL on at least one provocation test in a child who is short.

Overnight Growth Hormone Test. This evaluates a neurosecretory defect in growth hormone release. Individuals with growth hormone deficiency may demonstrate a normal growth hormone response in the setting of a stimulation test but without provocation cannot secrete adequate growth hormone to maintain growth. It involves measuring growth hormone levels every 20 minutes over a 10- to 12-hour period, preferably at night while the patient is sleeping. A growth hormone neurosecretory defect (a subset of GH deficiency) is defined as a mean growth hormone value of <4.2 ng/mL during the 12-hour overnight test in a child that is short.

Treatment

Growth hormone therapy is the treatment of choice for growth hormone deficiency (6–9). Growth hormone is dosed as 0.18 to 0.3 mg/kg/week divided into 6 injections per week. The injections are given subcutaneously at night, before bedtime. The patients are followed approximately every 3 to 4 months and receive a yearly set of thyroid function tests and bone age measures. The

side effects of this medication include alterations in carbohydrate tolerance including diminished insulin responsiveness and compensatory increases in insulin secretion, local tenderness and allergic reactions, short-term sodium fluid retention, and theoretical increased risk of leukemia 1:20,000 (10). Hypopituitary subjects may demonstrate growth hormone-induced hypothyroidism. Therefore, thyroid function tests are monitored regularly, particularly in individuals not growing well. The etiology for this is unknown. The cost in 1996 dollars per year is approximately \$10,000 to \$25,000, depending on the size of the child.

Growth Excess

There are just as many children greater than 2 SD above the mean as children below the mean, but there is typically less concern for tall stature. In addition, there are fewer pathological processes for tall stature (3). As with short stature, it is important to identify temporally the crossing of growth percentiles, disproportionate growth, or abnormal pubertal development. Most cases are familial and reflect the child's genetic potential. Other possible etiologies for growth excess include growth hormone excess, chromosomal disorders, sexual precocity, obesity, Soto's syndrome, and Weaver syndrome (see below).

Growth hormone excess is an extremely rare, treatable cause of tall stature in children. It results in pituitary gigantism in children and acromegaly in adults. The diagnosis may be confirmed with elevated somatomedin-C level (normal preadolescent range 60.8 to 724.5 ng/mL), increased prolactin and phosphate, and failure to suppress growth hormone after glucose load (1.75 mg/kg, up to a total of 100 gm). In normal subjects, growth hormone should be suppressed to <2 ng/mL. This excess in growth hormone may be accompanied by other pituitary hormonal causes. If growth excess is found, then referral is necessary. Surgery is the recommended initial treatment. Commonly used drug therapies in this disorder include bromocryptine and octreotide.

Common chromosomal disorders characterized by tall stature include Marfan's syndrome, homocystinuria and XYY syndrome. Precocious pubertal development may present initially as tall stature and early pubertal development. In this case, the bone age and height velocity should be advanced secondary to the overexposure to pubertal hormones. Soto's syndrome, cerebral gigantism, is characterized as large size at birth with excessive

growth during the first 4 years. The bone age is advanced. There is a distinctive constellation of associated features: high forehead, frontal bossing, high arched palate, mental retardation, and poor coordination. Weaver syndrome is characterized by macrosomia, accelerated growth and skeletal maturation, camptodactyly, developmental lag, and progressive spasticity.

PUBERTY

Normal Pubertal Development

In the United States, puberty begins between the ages of 8 and 13 in 98% of girls. For 98% of boys, puberty begins between the ages of 9 and 14 years. The normal sequence of the onset of pubertal changes in girls is increased height velocity, breast buds, growth spurt, pubic hair, genital maturation, and menarche (typically in Tanner stage 4; see below). The completion of puberty for females is 4.2 years (1.5 to 6 years). The normal sequence of the onset of pubertal changes in boys is testicular growth (98% of boys) with testes >2.5 cm in length, followed by pubic hair within 6 months, growth of penis and growth spurt. The completion of puberty for males is 3.5 years (2 to 4.5 years). The growth spurt is an early pubertal event in the girls and a late pubertal event for the boys. The onset of puberty is heralded by adrenarche, the increased secretion of adrenal androgens, mainly being dehydroxy-epiandrosterone (DHEA) and DHEA-S. Adrenarche typically begins at age 6 to 8 years for girls and boys. The persistent increase in adrenal androgens is necessary for gonadarche. Gonadarche marks the maturation of the hypothalamic-pituitary-gonadal axis with the increased secretion of luteinizing hormone and follicle-stimulating hormone (LH, FSH) (11–13).

Pubertal Maturation Scale by Tanner et al. (14)

Tanner Staging for Girls

- I. Prepubertal^{*}
- II. Pubic hair—sparse growth of straight or slightly curly hair, mainly on the labia; breast development—breast buds are visible or palpable
- III. Pubic hair—darker and coarse hair spreading over mons pubis; breast development—further enlargement of breasts and increased areolar, no separation of the contours

- IV. Pubic hair—thick adult-type hair, which has not spread on thighs; breast development—further maturation includes a projection of areola and papilla to form a secondary mound
- V. Pubic hair—classic inverse triangle; breast development—adult contour with projection of the papilla only

Tanner Staging for Boys.

- I. Prepubertal—testicular length <2.5 cm
- II. Pubic hair—sparse growth with slightly pigmented and curled hair, mainly at base of penis; genital development—testes of 2.5 cm in length, scrotum is thinning and reddening
- III. Pubic hair—thicker, curlier hair has begun to spread; genital development—penis grows in length and width, further testicular growth
- IV. Pubic hair—adult thickness, which does not spread; genital development—penis further enlarged, testes larger with darker scrotal skin color
- V. Pubic hair—hair spreads laterally; genital development—genitals adult size and shape

Delayed puberty

Puberty is considered delayed in boys if there is no initiation of secondary sexual development by 14 years of age. In girls, pubertal delay is considered if there is no initiation of secondary sexual development by 12 years of age. Etiology for delayed puberty can be divided into 3 categories: constitutional growth delay, hypogonadotropic hypogonadism, or hypergonadotropic hypogonadism. If delayed puberty is found, referral to an endocrinologist is appropriate.

A brief review of the 3 categories of delayed puberty is as follows (11–17):

Constitutional Growth Delay. This is characterized by delayed bone age, short stature but appropriate for the bone age, low but appropriate DHEA-S for bone age, normal karyotype, low gonadal steroids, low LH, FSH. Constitutional delay is often difficult to distinguish from hypogonadotropic hypogonadism early in its course. The DHEA-S may be helpful because in constitutional delay, both adrenarche and gonadarche are delayed, whereas in hypogonadotropic hypogonadism, only gonadarche is delayed.

Hypogonadotropic Hypogonadism. This is related to problems in the hypothalamus or pituitary causing insufficient release of LH, FSH. Typically, individuals with untreated hypogonadotropic hypogonadism demonstrate increased stature as adults.

There are many causes of this syndrome, including Kallman syndrome; congenital hypopituitarism; hypothalamic—pituitary tumors such as craniopharyngiomas (usually suprasellar); germinoma (growth hormone deficiency, diabetes insipidus, hCG [LH]); astrocytoma, glioma, histiocytosis X, and prolactinoma.

Other causes of hypogonadotropic hypogonadism include trauma, vascular and postinfectious inflammatory processes such as tuberculosis and sarcoidosis disrupting the hypothalamic-pituitary axis. Radiation therapy can also cause permanent damage to the pituitary and its ability for hormone secretion. Hormone deficiencies may not be manifest until 9 to 18 months after radiation therapy. Growth hormone deficiency is the most common pituitary deficiency followed by LH, FSH deficiency, adrenocorticotrophic hormone (ACTH) deficiency, and thyroid stimulating hormone (TSH) deficiency. Prader-Willi syndrome and Laurence-Moon-Biedl syndrome are functional syndromes characterized by incomplete or delayed puberty. Weight loss to <80% ideal body weight may cause a functional LH, FSH deficiency. Finally, major organ system failure of any kind, such as hypothyroidism, renal insufficiency, and cardiac disease, can cause delay in puberty. This delay may be secondary to the condition itself or to the suppression of growth hormone release commonly seen in chronic disease processes.

Hypergonadotropic Hypogonadism. As a cause of delayed puberty this entity is secondary to primary gonadal failure. The lack of negative feedback from the gonads causes an increase in LH and FSH. The most common example of this is Turner syndrome, in which the ovaries do not form properly. Klinefelter's syndrome is another genetic disease of gonadal failure in which there is seminiferous tubular dysgenesis. Differing from Turner syndrome, normal testosterone production occurs until about age 14 then progressive fibrosis of seminiferous tubules, eunuchoid proportions, and gynecomastia develop.

Acute causes of gonad failure include viral infection such as testicular mumps, coxsackie B virus, and autoimmune gonadal failure (polyglandular syndromes II and III). Chemotherapy with alkylating agents and radiation are frequently associated with go-

gonadal failure. Radiation exposure of <1000 rads causes permanent damage to ovaries; 1500 to 2000 rads causes permanent damage to testes with maintenance of normal testosterone production, 2500 to 3000 rads causes complete permanent gonadal failure in both the ovaries and testes.

Treatment for Delayed Puberty

1. Constitutional delay—reassurance; if patient is a male over 14 consider low-dose testosterone therapy in the oral form, halotestin 2 to 5 mg/d or testosterone enanthate 50 to 100 mg IM monthly \times 3 to 6 months; if female over 13, ethinyl estradiol 5 to 10 μ g/d or conjugated estrogen 0.3 mg/d. These low-dose preparations are used to facilitate the pubertal process but are not routinely recommended for individuals with a bone age <12 because of the potential effects on stature.
2. Hypogonadotropic hypogonadism—treat any underlying problem. For total gonadal replacement, begin testosterone at 50 mg IM and work up to 200 to 300 mg IM per month. The transdermal patch is best used once secondary sexual characteristics are established. For estrogen replacement, start at 0.3 mg/d for 3 to 6 months, then begin to cycle daily on days 1 to 21 at 0.3 mg/d conjugated estrogen, with medroxyprogesterone 5 mg/d, days 12 to 21. Increase the estrogen doses up to 0.6 mg, then 1.25 mg over the next 2 to 3 years unless fertility is an issue. In that case, hormones that can affect the maturation of the gonadal production of gametes are necessary. These include FSH (hMG [human menopausal gonadotropin]) and human chorionic gonadotropin (hCG, LH) for follicular rupture in females. In men, hCG is used initially to replace LH and produce the high intratesticular levels of testosterone that are needed for sperm production. In males who have secondary hypogonadism prior to puberty, hMG as well as hCG are usually necessary for fertility. The pulsatile administration of GnRH is an additional method to induce spermatogenesis in secondary hypogonadism due to hypothalamic rather than pituitary disease.
3. Hypergonadotropic hypogonadism—hormone replacement in similar doses as used in individuals with hypogonadotropic hypogonadism. These individuals are usually infertile.

Precocious Puberty

In boys, precocious puberty is defined as secondary sexual development before 9 years of age; in girls, secondary sexual development before 8 years of age. In the United States, precocious puberty affects about 1 in 5,000 to 10,000. The etiology is idiopathic in 80% of females, 35% of males. A central nervous system abnormality can be found in 66% of males. Precocious sexual development has some potentially serious etiologies and therefore must be evaluated promptly and referred to an endocrinologist. Once the more serious disorders have been ruled out, there are issues of ultimate short stature, and psychological and social issues. The first step in evaluating precocious puberty is to differentiate central precocious puberty from (peripheral) precocious puberty (13, 15).

Central Precocious Puberty

This is gonadotropin (LH, FSH) dependent and therefore is related to disorders of the hypothalamus and pituitary gland.

Peripheral Precocious Puberty

This entity is gonadotropin independent and may occur as a consequence of the exogenous steroids or gonadotropins; primary hypothyroidism with secondary elevation of FSH; ovarian tumors and cysts; congenital adrenal hyperplasia (untreated); adrenal tumors; McCune-Albright syndrome and autonomous hormone.

Combined Precocious Puberty

This generally begins as peripheral precocious puberty. With long-standing exposure to elevated levels of circulating androgens or other sex hormones, the hypothalamic-pituitary axis matures and begins to secrete LH, FSH, causing further pubertal maturation.

Variations of Normal Pubertal Development

Premature thelarche represents benign early breast development in girls without other evidence of pubertal development. It typically occurs between the ages 0 and 2 years and after 6 years. Breast development may be unilateral or bilateral. Absent in premature thelarche is estrogenization of vaginal mucosa, uterine enlargement,

growth spurt, or advancement of bone age. It is generally due to increased sensitivity to low levels of circulating estrogen or transient nonsustained increased estrogen from small ovarian cysts.

Premature adrenarche represents benign premature androgen secretion in girls and boys at pubertal levels. The child typically presents with early pubic hair development in the absence of other pubertal development. There is no appreciable virilization, accelerated height velocity, or advancement in bone age. Etiology of premature adrenarche is unclear.

Contrasexual Pubertal Development

This is defined as virilization in girls and feminization in boys. Potential causes of virilization in females include congenital adrenal hyperplasia, androgen secreting adrenal or ovarian tumor, polycystic ovary disease, Cushing's syndrome, hyperprolactinemia, hypothyroidism, and drugs. Laboratory evaluation should include testosterone and testosterone-binding globulin, prolactin, LH, FSH, and cortisol if Cushing's syndrome is a possibility. A testosterone level >200 ng/dL or DHEA-S >80 μ g/dL warrants imaging of the pelvis or abdomen. If prolactin is greater than 50 μ g/L on more than one sample, consider MRI of the pituitary gland. An ACTH stimulation test may be necessary to diagnose congenital adrenal hyperplasia, especially in the case of a partial defect.

Breast development in boys is a common physiologic pubertal finding occurring in 30% to 65% of boys. Typically, the boys are Tanner III-IV and the breast development is minimal, lasting only a few months. The etiology is unclear. Breast development and feminization in *prepubertal* boys is rare and requires evaluation for exogenous estrogen exposure and estrogen secreting tumors. The etiology of abnormal breast development in pubertal boys includes excessive estrogen production, deficient androgen production, and drugs. Tumors that produce estrogens include those of adrenal, testicular, and bronchogenic origin. Excess estrogen may also be seen in states of cirrhosis, congenital adrenal hyperplasia, thyrotoxicosis, and starvation. States of relative androgen deficiency include testicular failure, congenital anorchia, Klinefelter syndrome, androgen insensitivity syndromes, and defects in testosterone synthesis. A partial listing of commonly used drugs that may affect the balance of androgen/estrogen production is spironolactone, cimetidine, ketoconazole, chorionic

gonadotropin, antidepressants, marijuana, heroin, methyldopa, and isoniazid.

Evaluation of Precocious Puberty

One must first determine whether the origin is central or peripheral precocious puberty. The following are the initial points to be covered:

The history should cover overall health and energy level, progression of puberty and rate of pubertal development, headaches, nausea, vomiting, visual changes. Growth records should be available.

Physical examination should be complete with special attention to and documentation of primary and secondary sex characteristics, summarized as Tanner staging.

Laboratory studies include bone age, thyroid function tests, LH, FSH, estradiol, testosterone. If central precocious puberty is suspected, LH, FSH would be elevated. Peripheral precocious puberty is characterized by elevated testosterone or estrogen in the face of normal gonadotropins.

For premature thelarche the following additional data are appropriate: vaginal smear results, estradiol level, bone age. There should be follow-up every 4 to 6 months for 1 to 2 years. For premature adrenarche: DHEA, DHEA-S, 17-OH progesterone, testosterone; follow-up every 6 months.

The ACTH stimulation test may be necessary to determine the presence of congenital adrenal hyperplasia (Chapter 33). The GnRH stimulation test may be used to determine whether the pituitary is capable of a pubertal LH, FSH response.

X-ray. Imaging studies should be directed to the most likely source of hormone production; pelvic ultrasound for gonadal tumors, abdominal CT or ultrasound for adrenal tumors and MRI of the head for hypothalamic and pituitary sources. Several tumors of the CNS may cause precocious puberty. Choriocarcinomas, chorioepitheliomas and dysgerminomas can produce hCG, which has identical actions as LH. Hamartomas produce GnRH, and tumors of the pituitary may secrete LH (rare). In addition, space-occupying tumors such as neurogliomas, pinealomas, astrocytomas, craniopharyngioma, and histiocytosis X may cause precocious puberty by disinhibiting the hypothalamic control of puberty.

Treatment of Precocious Puberty

First, underlying causes are to be addressed and treated (i.e., surgery, radiation, medical management).

With idiopathic central precocious puberty, treatment depends on child's age, predicted adult height, and desire for therapy. Luprolide, a GnRH agonist, is an upregulator of gonadotropin releasing hormone. Chronic use of this potent agonist desensitizes the pituitary to GnRH and therefore stops production of LH and FSH. It is typically given as a monthly IM depot injection. Dosing in children begins at 7.5 mg. For height outcomes, continue this medication until the bone age is >12 years. Restoration of LH, FSH occurs within a few months of discontinuation of the medication. Monitoring therapy includes periodic bone age evaluation and LH, FSH measurements to ensure suppression.

Peripheral precocious puberty is independent of gonadotropins. Therefore, GnRH agonists would not affect the pubertal development. Androgen antagonists including cyproterone acetate, medroxyprogesterone acetate, testolactone (McCune-Albright syndrome), spironolactone, and ketoconazole may decrease sex steroid secretion or action. Cyproterone acetate blocks the estrogen/androgen receptor sites. Ketoconazole blocks the conversion of C-21 steroids to C-19 steroids. Medroxyprogesterone acetate partially blocks LH, FSH as well as the production of estrogen and testosterone. Testolactone inhibits the conversion of androgens to estrogens. Spironolactone inhibits synthesis of androgens via the cytochrome P450 system.

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Allergies

Chapter 35

Atopic, Food, and Contact Allergies

William A. Schwer

ATOPIC ALLERGY

Symptoms occurring immediately after allergen exposure are related to the interaction of IgE bound to the surface of mast cells with IgE specific allergens. The cross-linking of the IgE molecules by the allergen leads within minutes to the release of a number of mediators of the immune response by mast cells. Vascular leakage, smooth muscle contraction, and other responses produce the symptoms dependent on the area where the mast cells are located. Mast cells so stimulated in the bronchial tree produce rapid smooth muscle contraction or bronchospasm and edema. Mast cells in the gastrointestinal tract produce increased peristalsis with resultant vomiting, diarrhea, and cramping. Mast cells located in the skin can produce erythema, swelling, and pruritus. These symptoms all are related to the immediate type hypersensitivity. It is clear that the true pathophysiological basis of atopic diseases is

the observation that they are chronic inflammatory diseases. This is best reflected by the early and late phase asthmatic response (1). In allergic subjects undergoing inhalation challenge a rapid decline in pulmonary function would develop, which would rapidly (15 to 30 minutes) reverse spontaneously. In approximately 50% of subjects with bronchospasm, a recurrence of the bronchospasm would develop from 3 to 8 hours after the initial response (2). This late asthmatic response was frequently more severe than the initial bronchospastic component. It was much longer in duration and fairly refractory to beta adrenergic drugs related to its essential inflammatory as opposed to functional nature.

A similar delayed response can be seen with allergic skin tests. In patients having a positive skin test to an allergen, 30% to 50% of these patients had a recurrence of the erythema and induration following the total clearing of the initial response. Again the late skin response was generally greater in size and lasted much longer than the early response (up to 24 hours) (3). Similar late phase responses can be elicited from allergen challenge to nasal mucosa and the conjunctiva.

Late phase responses closely resemble the actual clinical presentations of allergic disease. In asthma, bronchospasm is seen in both the early and late phases. Only the last phase is associated with significant pulmonary function changes such as air trapping. The last phase asthmatic response closely resembles its disease counterpart in its treatment with antiasthma therapies. The last but not the early phase can be prevented with pretreatment with inhaled steroids. Also immunotherapy suppresses the late phase but not the early phase response. Although the bronchodilatory drug effects both early and late phase, bronchodilation is much less predictable in the late phase.

The immediate response of the skin to allergen challenge is only associated with vascular leakage and edema. However, biopsies of the skin during the late phase show an inflammatory response characterized by the presence of basophils, eosinophils, monocytes, and lymphocytes.

Patients who only have an early phase response to inhaled allergens do not develop bronchial hyperactivity. An increase in bronchial hyperactivity precedes the late phase response and may persist for up to 6 weeks (4).

What is important to appreciate is that in asthma the allergen dose presented to the patient in nature is many times smaller

than in the laboratory. Therefore, the acute phase of bronchospasm may not be evident. However, even small doses of the allergen may produce the late phase response. The locally destructive inflammatory response will persist for weeks after exposure. Eventually, the cumulative effects of the deposition of allergen throughout the airways will produce the pathophysiologic presentation of asthma. Thus, asthma may develop without any identifiable causative agent. The chronic exposure to the allergen that leads to chronic inflammation may eventually produce symptoms that obscure the early response. As with acute reactions, the clinical manifestations of late phase inflammation depends on the tissue in which they take place, leading to allergic rhinitis, asthma, atopic dermatitis, chronic diarrhea, or, in children, failure to thrive.

The recent observations that inflammation plays a more critical role than do immediate responses in the pathogenesis of allergic diseases has caused a shift in treatment guidelines to emphasize the role of allergen elimination from the environment and the earlier introduction of anti-inflammatory therapy.

Atopic Dermatitis

Atopic dermatitis is an intensely pruritic, erythematous, maculopapular eruption of characteristic distribution that progresses to excoriated and dry lichenified lesions of the skin. The disease is of early onset, there is generally a family history of atopy, and elevated IgE concentrations are seen in the skin. Chronic lichenified lesions exhibit increased numbers of fully granulated mast cells, lymphocytes, monocytes, and Langerhan cells (5). The cutaneous manifestations of atopic dermatitis have distribution patterns that vary with age (6).

The infant phase, up to 2 years of age, is characterized by dry, erythematous scaly plaques, often called infantile eczema. These are confined to the cheeks, abdomen, and extensor surfaces of the legs. Pruritus, which is the prominent symptom, can present as irritability or sleep disturbances.

The childhood phase, from 2 to 12 years, is characterized by papules, which coalesce into plaques in the flexor areas of the neck, antecubital, and popliteal fossae, as well as the wrists and ankles, reminiscent of the time honored description of "nummular eczema," or nummular neurodermatitis.

In the adult phase, the lesions are more diffuse, have greater scaling, and involve the dorsa of the hands, upper eyelids, and the flexor surfaces of extremities.

The diagnostic criteria consist of the intense pruritis of the rash, its distribution and morphology, and its chronic or relapsing course.

Eighty percent of patients with atopic dermatitis exhibit symptoms by the age of 1 year, and greater than 90% have symptoms by age 5. The incidence is between 2% and 5% in the United States. Patients with mild disease will clear permanently by age 20 in 75% of the cases. Patients with more severe disease will have a chronic course all of their lives in 75% of the cases.

Food hypersensitivity, which will be presented separately, has been postulated to be one of the causative agents in atopic dermatitis. A number of elegant experiments have shown that there is some relationship. However, contrary to popular belief, patients with atopic dermatitis are not allergic to a large number of foods. Although most patients have several positive skin test results and RASTs, greater than 75% of all children are sensitive to only one or two foods. Only 3% of all children are sensitive to four or more different foods. The type of food the parents thought caused allergic symptoms was not predictive of which foods actually elicit a positive oral food challenge (7).

Treatment for atopic dermatitis consists of controlling precipitating factors and of local therapy. In infancy, because of the likelihood that food or wool sensitization is a stimulant for the dermatitis, an attempt should be made to identify the causative agent(s) by skin tests. Since eggs, milk, and wheat are the most likely food sensitizers, it is common to place the infant on a diet that eliminates one or more of these routinely for the first 6 months of life and for the first year in those with family histories of atopic diseases. In adults, allergens that may produce positive skin patch results should be eliminated if possible.

Local therapy consists mainly of corticosteroid creams, ointments, or lotions. Topical antihistamine preparations should not be used for any prolonged time. Tar-based ointments also can be used, but patients typically do not care for the odor or staining of clothing.

Oral antihistamine and cyproheptadine are regularly used to reduce the severe pruritis associated with the plaques. In severe disease, rapidly tapering corticosteroids are used with great success.

Allergic Rhinitis, Conjunctivitis (Hay Fever)

Allergic rhinitis is characterized by nasal irritation, sneezing, and rhinorrhea following exposure to the relevant allergen. Major features of allergic rhinitis during seasonal exposure include nasal epithelial mast cell proliferation, and increased numbers of eosinophils and basophils. Eosinophil numbers in nasal secretions also increase during seasonal exposure and within hours after an allergen challenge. Nasal eosinophilia persists for at least 10 days (8). Approximately 20% of the U.S. population will during their lifetime develop allergic rhinitis (9).

Patients should be asked about any precipitating factors such as pollens, dust, molds, and animal derived proteins that cause an IgE mediated reaction. Other irritants, such as perfumes, paint, tobacco smoke, and air pollutants may cause irritant non-allergic responses that mimic allergic disease. Changes in temperature, humidity, and barometric pressure may also induce rhinitis. Approximately 60% of patients with allergic rhinitis have a positive history of allergy.

The popularity of obtaining nasal smears to detect eosinophils has declined. The smears are usually obtained by asking the patient to blow the nose into plastic wrap. The main clinical utility of cytology is to differentiate infections from allergic rhinitis. Neutrophils are seen in the former and eosinophils are seen in the latter. The absence of eosinophilia does not rule out an allergic etiology. Patients with nasal eosinophilia respond to topical nasal steroids.

Prick skin testing with appropriate antigens remains the most useful procedure in determining triggers associated with allergic rhinitis. Skin testing is rapid, specific, and sensitive, particularly in adults. Positive skin prick tests that correlate with the clinical history are of value in confirming IgE mediated reactions.

Seasonal allergic rhinitis (hay fever) includes nasal and ocular symptoms occurring during well-defined seasons. It is caused by an IgE mediated reaction to inhalant pollen allergens leading to mediator release, which causes mucosal edema, vasodilation, sneezing, itching, rhinorrhea, and lacrimation. It affects approximately 10% to 15% of the population. It is equally common in both sexes. It is most likely to be symptomatic between the ages of 15 and 25 years and decreases in middle age.

Seasonal allergic rhinitis is most commonly caused by pollens and mold spores. The pollens and molds are deposited on the nasal mucosa. The amount of allergen in the air correlates well

with rhinitis symptoms. Ragweed is the most common cause in North America. This pollen occurs commonly between August and October. Rain and high wind speeds lead to low pollen concentrations. Mold spores are released into the air when lawns are disturbed by mowing or the raking of leaves. Damp conditions inside the home encourage the growth of molds.

Antihistamines are generally used as first-line treatment for allergic rhinitis. Antihistamines are primarily helpful in controlling sneezing, itching, and rhinorrhea but do not relieve nasal blockage. The symptomatic relief of allergic symptoms may last up to 12 hours or longer with newer agents. Tolerance to antihistamines does not occur, and compliance is considered to be the major factor in treatment failures (10).

The most common side effects of antihistamines are sedation, dryness of mouth, and impaired performance. The sedation can be reduced by using a decongestant in conjunction, or by using nonsedative second-generation antihistamines such as terfenadine (Seldane) or astemizole (Hismanal). The new agents loratidine (Claritin) and cetirizine (Zyrtec) have the added advantages of safety when taken with macrolide antibiotics.

Cromolyn sodium inhibits allergen-induced degranulation and mediator release from sensitized mast cells. It prevents both the early and late phase reactions. It is most effective in controlling sneezing, rhinorrhea, and nasal itching. It is not as effective with nasal congestion. For effective topical nasal use, the medication must be used at least four times daily. Cromolyn may cause sneezing or nasal stinging in a few patients.

Corticosteroids are the most effective medications for allergic rhinitis treatment. They are used intranasally, but may be used orally to control severe symptoms. Intranasal steroids inhibit medication release for mast cells and basophils. They reduce edema of the nasal mucosa. They lack systemic side effects. Nasal steroids also reduce inflammation, suppress neutrophil chemotaxis, and decrease late responses to nasal allergen challenge. They are long acting and can be used once or twice daily. They should be used regularly rather than taken only as required. Some patients may complain of nasal irritation, nasal burning, drying, and epistaxis. Epistaxis occurs because of the drying and responds to cessation of the spray for several days. The therapeutic effect may take several days to develop. Maximum effect is usually seen within 2 to 6 weeks.

Nasal saline acts as a mild decongestant, soothes irritated mucosa, liquifies mucus, and prevents dryness. Saline is usually administered as a nasal spray 2 to 4 times daily.

Immunotherapy is the subcutaneous administration of increasing doses of the allergens in which the patient is sensitive. Immunotherapy should be considered in patients who cannot control symptoms with environmental manipulation and medications. Appropriate immunotherapy increases patient tolerance to natural exposure to a specific aeroallergen. It decreases the severity of symptoms and medication requirements.

Skin prick testing, the prerequisite for immunotherapy, is the most useful diagnostic test for an allergy. It can be performed safely and rapidly. Properly done, skin testing is a highly sensitive and relatively inexpensive test. Skin testing will answer two questions: 1) does the patient have an allergy, and 2) which are the allergens causing the reaction. Therefore, the cornerstone of allergic disease, including asthma, is the identification of allergens to which the patient is sensitive and then the elimination of those allergens from the patient's environment.

Immunotherapy produces increases in specific IgE blocking antibody to allergen, reduces specific IgE antibody levels, blunts the usual seasonal increase in IgE levels, reduces mast cell and basophilic degranulation, and stimulates T-lymphocyte suppression of IgE production (11).

The immunotherapy is usually discontinued after 4 to 5 years of good compliance with a steady regimen. Approximately 60% of patients maintain clinical improvement after stoppage. The patient should be re-evaluated after 1 year for modification or discontinuation of immunotherapy if there is no significant improvement in clinical symptoms.

The following is an example of how diagnosis and desensitization can be performed in the office.

Immunotherapy (Desensitization)

Extracts of the common airborne antigens are placed in individual droplets on the glabrous skin of the forearm or the back (more likely in a child or a smaller person). The skin is pricked through the droplet, penetrating enough to be able to pick up a small fold by rotating the needle nearly 90 degrees on its midpoint. IgE antibodies involved in rhinitis or asthma result in an immediate reaction, so that a positive test consists of a palpable

wheal, which may be found at the site within 10 to 15 minutes. Macular erythema at the site does not constitute a positive test. Commercial laboratories are available that will mix various dilutions of the antigen(s) in a "vaccine," for serial injection. Pollen desensitization is most effective; dust intermediately so, and animal danders least so and most fraught with complications.

As originally designed, a typical schedule, beginning 3 months in advance of the season, consisted of serial weekly injections increasing in volume from 0.1 mL of a "vaccine" containing a highly diluted solution of the allergen(s) (e.g., 1:1000 or higher) that, by seasonality and skin testing, was known to be the cause of clinical symptoms. Subsequent vials would contain concentrations each 10 times the previous one, for a total of three or four vials. The off-season could be maintained by less frequent injections of the highest dilution, perhaps 1:10. The frequency is generally accelerated to weekly once the season of symptoms has cycled around in the following year. Alternatively, the shots may be stopped for the off-season, and the whole program started prior to the following season anew.

In recent years, allergens for immunotherapy have been prepared according to the strength of their allergenicities as measured in units. These range in vials from 1 to 500 units, for example, in one injection volume. The extracts are now standardized according to FDA requirements.

Asthma

Bronchial asthma is a disease characterized by reversible airway obstruction and airway hyperresponsiveness. Airway inflammation is the primary mechanism for both of these characteristics. The bronchi are characterized by edema, an increase in goblet cells, basement membrane thickening, and smooth muscle hypertrophy and hyperplasia. Mast cells, T-lymphocytes, and eosinophils are present in the subepithelial layer, and the inflammatory exudate contains many eosinophils. Bronchial biopsy in chronic stable asthma reveals epithelial injury ranging from minor disruption of the epithelium to complete denudation of the epithelium. The bronchial obstruction of asthma results from bronchial wall edema and plugging of the airways with mucus and inflammatory debris, and only to a lesser extent from smooth muscle contraction.

Respiratory infections increase asthma severity in many patients. Furthermore, it has been observed that airway responsiveness increases in asthma during a viral respiratory infection and may persist for months beyond the initial viral illness. Bacterial infections of the respiratory tree seldom cause exacerbation of asthma. The influence of viral respiratory illnesses on asthma appears to be dependent on several factors. First, children younger than 5 years of age appear to be at greater risk for developing increased wheezing with a viral respiratory illness. Second, a family history of allergic disease was more frequent in children who eventually experienced one or more episodes of wheezing with colds. Third, certain pathogens such as respiratory syncytial virus (RSV), parainfluenza virus, rhinovirus, influenza virus, and *Mycoplasma pneumoniae* are the most likely to provoke asthma. Fourth, the more severe the respiratory illness, the more likely wheezing is to occur. Fifth, boys have a greater tendency to wheeze with the viral respiratory infection than girls. Sixth, the more severe the asthma, the more likely that patients will wheeze with colds.

It appears that viral respiratory infection has a greater and longer lasting effect on the factors involved in the development of the late phase asthmatic response than does bacterial infection. The events that relate to or determine the late phase reactions are particularly susceptible to the effects of respiratory viruses.

Allergic asthma may be manifested as wheezing, coughing, or exercise intolerance. The sensitization of children appears to be the major risk factor for asthma. Although sensitization to food allergens may decrease with age, sensitization to inhaled allergens increases in atopic children as they get older. Early sensitization to indoor allergens such as mites, cockroach, cat and dog dander, and molds may predispose to subsequent sensitization to outdoor allergens. Thus, early recognition of allergic symptoms and early intervention such as immunotherapy and removal of offending agents are an important part of the early management of asthma.

Immunotherapy has proved effective in asthma, particularly in patients with reactivity to a single or only a few allergens. This should be used only after preventive measures and reasonable drug treatment fails. In actuality, few children require immunotherapy.

The treatment of asthma has evolved significantly to now concentrate on the management of the inflammatory or late phase re-

actions rather than the bronchoconstriction seen in the early phase. As a result, bronchodilators, long a mainstay of treatment, now can be used, based upon frequency, as an indication for anti-inflammatory therapy. Therefore, the goals of asthma therapy include 1) to bring about resolution of the inflammatory process in the airways, with consequent improvement in pulmonary function and reduced airway hyperresponsiveness; 2) to protect the airways from irritant stimuli and to prevent the pulmonary and inflammatory responses to an allergen; and 3) to provide a bronchodilator effect to relieve bronchospasm. The individual medications may be grouped into those that are considered nonbronchodilator anti-asthma medications (cromolyn, nedocromil, glucosteroids) and those that are primarily bronchodilators (beta-adrenergic agonists and theophylline). Response to therapy can be measured in the office or at home by spirometry or peak flow meter.

Nonbronchodilator Antiasthma Medications

Cromolyn blocks both the early and late phase pulmonary response to allergen challenge and *prevents* the development of airway hyperresponsiveness. Its primary advantage is the minimal incidence of adverse effects, which makes it a safe medication for all age groups. It seems to be particularly effective in children. While cromolyn appears to be an effective mode of therapy in the treatment of mild to moderate asthma, cromolyn adds little to the treatment of severe asthmatic patients in the presence of steroid therapy.

Nedocromil also blocks both the early and late phase pulmonary responses to allergen challenge. It is also particularly effective for mild and moderate asthma. Cromolyn seems to be more effective for night-time asthma.

Steroids represent the most potent agents for the treatment of asthma. They block the late phase pulmonary response and the development of airway hyperresponsiveness. Continued administration of inhaled steroid therapy is also effective in blocking the early phase response. Inhaled steroids are more effective than beta agonists, cromolyn, or theophylline in reducing airway hyperresponsiveness during maintenance treatment. Only nedocromil provides a similar significant and sustained decrease in airway hyperresponsiveness (12). Severe acute asthma is treated with systemic steroids combined with frequent administration of inhaled beta agonists.

Beta adrenergic agonists as a group have evolved from short acting with nonbeta selectivity (epinephrine, metaproterenol) to those that last longer with greater beta-2 selectivity (albuterol, terbutaline, pirbuberol) to ones that have high beta-2 selectivity and long duration of action (salmeterol). Their greatest advantage is a rapid onset of action in the relief of acute bronchospasm via smooth muscle relaxation and increased mucociliary clearance. They are also excellent broncho-protective agents for pre-treatment prior to exercise.

Salmeterol, as opposed to shorter acting beta agonists, blocks both the early and late phase reactions in asthma and its effects can last up to 30 hours after a single dose. It is also 50 times more beta-2 selective than albuterol.

In the past anticholinergics have had limited application in the treatment of asthma. Ipratropium (Atrovent) has the ability to potentiate beta agonist effects and lengthens their effectiveness from 4 hours to 6 hours and also adds between 10% and 15% improvement in symptoms. They should be used in cases of severe chronic asthma after steroids and beta agonists have already been implemented.

In the past, theophylline was used in asthma, but because it is a much weaker bronchodilator than beta agonists, has a narrow therapeutic range, its use has fallen out of favor. It does help to attenuate both the early and late phases of asthma. This is related to its ability to decrease microvascular leakage and macrophage activity.

FOOD SENSITIVITY

The first allergens encountered in an individual's life are food allergens. It is known that the fetus continually swallows amniotic fluid, which contains proteins found in the maternal diet. Infants become sensitized to food proteins in breast milk or commercial formulas. Cow's milk, soy formula, wheat, peanut proteins (present as an additive factor in other foods), and eggs are the most important allergens in early infancy. During late infancy and early childhood, vertebrate fish, shellfish, and tree nuts are common food allergens. Foods frequently claimed to cause an allergic phenomenon such as strawberry, tomato, corn, and chocolate rarely elicit an allergic response in a controlled setting.

When a food challenge reaction is positive, it occurs within 10 to 90 minutes after oral intake. Cutaneous reactions occur in

approximately 80% of the patients, consisting of pruritis and an erythematous macular rash. Gastrointestinal symptoms, characterized by nausea, vomiting, abdominal pain, and diarrhea, occur in greater than 40% of the reactions. Respiratory symptoms such as wheezing, congestion, sneezing were induced in almost 30% of the challenges.

Clinical food hypersensitivity is very specific and usually does not cross members of a botanical family or annual species. Consequently, the common practice of avoiding all legumes when a patient is allergic to peanuts, or chicken if the patient is allergic to eggs, appears unwarranted and nutritionally unsound. Adherence to a food elimination diet is often difficult, and therefore a diet restricting as few foods as possible is most successful.

Once food hypersensitivity is diagnosed the patient is placed on a diet strictly avoiding the offending food allergen. After the food allergic child is placed on the appropriate diet, there is a marked and rapid improvement in the patient's symptoms (dermatologic, gastrointestinal or respiratory) in most cases. Other therapies for food hypersensitivity such as oral desensitization immunotherapy, and rotational diets have never been shown to be effective in controlled studies and are not useful.

In the evaluation and management of food hypersensitivity, physicians must be cognizant that the publicity surrounding food allergies has clouded the issue. Physicians should be aware that parents may institute bizarre and nutritionally deficient diets. Much remains to be learned about the specifics of symptoms, diagnosis and mechanisms of food hypersensitivity disorders.

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Preventive Care, Health, and Efficiency

Chapter 36

Preventive Care, the Patient, and the Doctor

Daniel J. Bloch and Glen F. Aukerman

Keeping people healthy is an admirable goal. A goal mentioned too rarely in medical training. A goal that the public does not always seem to embrace, favoring high-technology cures for rare illnesses. Prevention is the quintessence of what the family physician does. A goal that the U.S. Public Health Service has articulated in *Healthy People 2000*, with the aims of increasing the span of healthy life for Americans, reducing health disparities among Americans, and achieving access to preventive services for all Americans.

DOCTOR-PATIENT RELATIONSHIP

Nowhere in medicine is the doctor-patient relationship more important than in prevention. Nowhere in medicine is the doctor-patient relationship more important than in family practice.

The things that we tell patients to do to maintain their health are frequently unpalatable to them. The benefits of doing those things are usually far in the future. To persuade a patient that a lifestyle change is valuable may be very difficult. It is virtually impossible in the absence of a collaborative relationship between doctor and patient. What sets family medicine apart from other specialties is that, for the family physician, continuing the relationship with his/her patient is an integral, not incidental, part of medical practice.

HEALTH MAINTENANCE VERSUS PREVENTION

Prevention of disease is an old concept. Maintenance of health is a newer one. The two are not synonymous.

The "annual physical" is a relatively new creation, invented by the AMA in 1922; it was intended to detect early manifestations of illness. It failed in this purpose because most illnesses aren't detectable at a presymptomatic stage, and because the ones that are detectable are frequently not changeable (much less curable). Instead, we now advise a periodic examination (usually not annual) focused on appropriate interventions. However, "The Complete Annual Physical Examination Refuses To Die" (1) for several reasons:

Doctors' reluctance to accept limitations of some screening tests.
Patients' expectations.

Perceptions of the importance of the examination in doctor-patient relationship.

Habit.

Malpractice phobia.

Pecuniary motivation.

The preponderance of deaths in people up to age 45 have been caused by misadventure, not illness; most "disease" likewise. Therefore, counseling someone who is asymptomatic on how to avoid violence, for example, is more likely to be beneficial than measuring a potassium level. For that matter, counseling a 65-year-old man who is asymptomatic to avoid driving while intoxicated is more likely to be beneficial than measuring a PSA level. How can this be? Doctors are trained to look for illness. Patients, however, are more likely to benefit from changes in lifestyle. Physicians may need to change their focus from the "glamorous" detection of prostate cancer to the "mundane" prevention of a drunken-driving death.

If we reduce a man's cholesterol level by 1%, we reduce his risk of dying of coronary artery disease by 2%. But if the man is 40 years old and has no other coronary risk factors, the absolute risk reduction may be seen as clinically insignificant. The 40-year-old's risk of ever dying of coronary artery disease is about 10 in 100; a 2% reduction in that risk makes it 9.8 in 100, so we must lower 500 such patients' cholesterol by 1% to prevent one death.

If we persuade a 40-year-old man to discontinue smoking, we reduce his risk of dying of coronary artery disease by 30%. His risk starts out at 20 in 100; a 30% reduction in that risk makes it 14 in 100, so we only have to persuade 17 such patients to quit smoking to prevent one death. So which is more effective? Clearly, the targeted approach to the at-risk patient will save more lives than blanket intervention to deal with abnormal laboratory values.

Patient Education

A great deal of health maintenance is carried out by patient education. Traditionally this has been a haphazard matter of one doctor telling one patient to quit smoking, another to lose weight, etc.

More recently, patient educators have sprung forth: medical professionals (frequently nurses) who teach patients how to keep themselves healthy. The patient educator sometimes educates like a traditional schoolteacher; he or she may also create or select patient-education materials, such as pamphlets, videotapes, or computer programs. The patient educator might work individually with one patient or might conduct classes, perhaps with all the diabetic patients in one doctor's or one group's practice. Since patient educators are not as expensive as doctors, and since the education frequently is in a group setting, this form of prevention should be more cost-effective than the traditional one-doctor-one-patient method.

More recently still, public-health workers have taken on the challenge of educating entire populations. Studies have shown some benefit from community education campaigns to decrease smoking prevalence. But probably most of the reduction in smoking in the past 20 years has come from changing public opinion, rather than through the efforts of public-health authorities. Likewise, driving under the influence of alcohol has become less stylish, more as an effect of shifting mores than an effect of doctors' pronouncements.

On the other hand, increased use of seat belts is clearly a consequence of increased enforcement of laws requiring such use. These laws did originate with the efforts of public-health workers, concerned over the high death rate in children in motor vehicle accidents.

PREVENTION VERSUS SCREENING

Prevention (Preventing the Onset of a Pathological Process)

Primary Prevention

Primary prevention of tetanus involves keeping individuals from suffering cuts and immunizing everyone against tetanus.

Primary prevention of coronary artery disease involves prevention of the development of asymptomatic atherosclerosis, by maintaining normal cholesterol levels, avoiding tobacco use, and keeping weight and blood pressure normal, and increasing exercise.

Secondary Prevention (Prevention of an Asymptomatic Process From Becoming Symptomatic)

Secondary prevention of tetanus involves postexposure tetanus immunization, after a cut is sustained.

Secondary prevention of coronary artery disease involves detection of asymptomatic atherosclerosis and treating it to prevent the patient developing his/her first myocardial infarction.

Tertiary Prevention

This is prevention of progression or recurrence of a symptomatic process; although it is customary to call this "prevention," this is more like treatment.

Tertiary prevention of tetanus involves treating the patient who has developed tetanus infection after being cut.

Tertiary prevention of coronary artery disease involves preventing the patient who has had a first myocardial infarction from having a second.

Screening

By analogy to prevention, one can imagine primary, secondary, and tertiary screening. Screening detects that which prevention proposes to avoid.

Primary screening detects the elevated cholesterol level or the tobacco abuse in the patient without coronary artery disease.

Secondary screening detects the patient with asymptomatic atherosclerosis before the first myocardial infarction.

Tertiary screening detects the prior myocardial infarction.

Traditionally, "screening" has meant detecting disease in the asymptomatic person (secondary screening, as defined above). This, clearly, is not quite the same as prevention. This sort of screening is also not nearly so effective as primary screening. Thus, current recommendations for screening tend to emphasize such primary (and unglamorous) measures as counseling patients about their health habits, rather than performing wholesale coronary arteriography to detect presymptomatic atherosclerosis.

Prevention in Populations Versus Prevention in Individuals

Some interventions are more effective on a population basis than an individual one. For example, if we convince one patient not to go home and shoot her husband, we make an immediate and significant impact on those two individuals, and save one or two lives. If we immunize all the children in the United States against poliomyelitis, we will save tens of thousands of lives. But most individual children in the United States will not benefit, because most would never have caught polio in any event.

Likewise, if we lower one person's cholesterol by 1%, he may be one of the 95% people with high cholesterol who would never develop coronary artery disease. But if we lower the cholesterol of every man in the United States by 1%, we prevent 2% of the myocardial infarctions that that population would have had. Thus, we prevent 15,000 myocardial infarctions this year, of which 5,000 would have been fatal.

Prevention in Minorities

Immunization against polio was nearly complete in the United States by 1963. However, in Nigeria, even in 1996 the majority of children are not immunized. And, even in the United States, inner-city populations are much less completely immunized than suburban populations. Minority populations have considerably different prevalences of disease; diabetes is extraordinarily common in Native Americans, very common in African-Americans, and rather uncommon in Asian Americans. Prostate

cancer occurs more often and earlier in African-Americans than in whites.

GENERAL PRINCIPLES OF PREVENTION

The foregoing discussion should make it clear that a physician cannot apply screening measures to all patients, regardless of the disease to be screened for and regardless of the patient's risk. The concepts of burden of suffering and of futility can help us to choose which interventions are worthwhile.

Burden of Suffering

This term encompasses both severity and prevalence. We should try to prevent conditions that have a large burden of suffering, either for the population as a whole or for the individual patient. If an illness affects one person in a million, expending effort to prevent it may not be worthwhile. If an illness causes minimal discomfort and no disability, even if it is common, you might choose to prevent something else, instead.

Futility

For some conditions, there is no available treatment; for others, there is no effective treatment.

For some conditions, treatment produces remission or other objective improvement, but that improvement is not translated into improved morbidity or mortality. Screening for such conditions is unlikely to be beneficial.

THE SCIENCE OF PREVENTION

If you screen for a very rare condition, not only are you unlikely to find any cases of it, but you are quite likely to find false-positive results. If your patient is highly likely to have a condition before you screen for it, the result of the screening test may not alter that likelihood. Therefore, to avoid wasted effort, it is good to understand the basic scientific terminology and principles outlined below.

Prevalence and Incidence

Prevalence is what proportion have it now. Incidence is what proportion develop it over a period of time. Using the definitions in

the table, we can calculate some very useful derived terms. These terms help to characterize a potential screening test; depending upon the circumstances, one might choose a test with a high specificity over one with high sensitivity (it is uncommon for one test to be both highly sensitive and highly specific). Knowledge of a test's positive and negative predictive value (PPV, NPV), combined with knowledge of the prevalence of the condition being sought, can enable one to compare the pretest probability that the patient has a disease with the post-test probability. If the odds of disease are 10% before the test and 8% after it, one has gained little information.

	Condition Present	Condition Absent
Positive Test	a (true +)	b (false +)
Negative Test	c (false -)	d (true -)

Specificity

$$\frac{d}{b+d}$$

Use a highly specific test to rule *in* a disease, because it will have few false-positive results.

Sensitivity

$$\frac{a}{a+c}$$

Use a highly sensitive test to rule *out* a disease, because it will have few false-negative results.

Positive Predictive Value

$$\frac{a}{a+b}$$

If PPV is high, a patient with a positive test is highly likely to *have* the condition.

Negative Predictive Value

$$\frac{d}{c+d}$$

If NPV is high, a patient with a negative test is highly likely *not* to have the condition.

Bayes Theorem

This theorem is what connects the specificity, sensitivity, positive predictive value, and negative predictive value. It isn't enough to know how "good" your test is. You must also stop and think about the likelihood that your proposed diagnosis is correct. No test, no matter how "good" it is, can relieve you of the responsibility of formulating hypotheses about your patient's problem. The general public is easily gulled by glowing reports of the latest new miracle screening test that will detect "cancer" without the need for a doctor's involvement. If the general public were aware of Bayes theorem, they would be less easily fooled.

The following example is oversimplified but illustrative.

Assume a condition with a prevalence (in your patient population) of 1 in 10,000. Suppose there is a test for this condition with a false-positive rate of 1%. In other words, its specificity is 99%, which is quite good. Then there will be 100 false-positive tests in 10,000. Suppose the test, luckily enough, happens not to miss that one patient in 10,000 who has the condition. Now you've got 101 positive results, only 1 of which is in a patient with the disease. So 100 out of 101 positive results are falsely positive. So your positive predictive value is $<1\%$, which is quite poor. So you probably shouldn't have used that test to screen for that condition in your population.

Efficacy Versus Effectiveness

An efficacious test *can* detect the condition accurately. An effective test *will* favorably impact the patient's survival or health in actual clinical use.

Biases

Any screening test may be influenced by bias. Some biases tend to make the test look more efficacious than it is; others may make it appear less efficacious. Some efficacious tests are ineffective be-

cause of biases introduced in translating the test from theory to practice. Bias does not invalidate the test, but it must be considered when evaluating the test's utility. In some instances, one screening measure is recommended over another because the recommended one is less subject to bias.

Length Bias

Refers to the falsely apparent early stage of development in which a dormant or indolent condition may be discovered in a screening program.

Lead-Time Bias

This refers to a false apparent increase in survival after discovery at screening, of a condition that otherwise kills at the same absolute point in time. As an example, assume your patient has a cancer that will kill her on Jan. 1, 1999. Suppose you discover that cancer by screening on Jan. 1, 1997. The patient survives 2 years with the cancer. If, without screening, the patient discovers her cancer on Jan. 1, 1998, when it causes symptoms, the patient survives only 1 year with the cancer. While it appears that screening increased the patient's survival by 1 year, it merely increased the length of time that the patient was aware of the cancer.

Selection Bias

This refers to the fact that the population that makes itself available for screening may have other characteristics that confer upon it greater longevity. Thus, their increased health is the result of the patients' lifestyles, not of screening.

EVALUATION OF RECOMMENDATIONS

Screening recommendations from the U.S. Preventive Services Task Force are graded (A through E) on their strength. The scientific evidence may be strong or weak, and the evidence may suggest performing or not performing the screening measure:

Code	Strength of recommendation	Should the measure be performed?
A	good	yes
B	fair	yes

C	poor	ad lib; no strong evidence either for or against performing the test
D	fair	no
E	good	no

Quality of Evidence

The Task Force also assesses the quality of the studies upon which its recommendations are based, assigning a code (I through III, with subtypes of II) based on the characteristics of the trial or source of the recommendation.

Code	Randomized trial	Controlled trial	Description of evidence
I	yes	yes	
II-1	no	yes	
II-2	no	no	cohort, case-control study
II-3	no	no	dramatic, historical evidence
III	no	no	expert opinion

Cost Considerations

Reimbursement for preventive care has been problematic. Traditional reimbursement schemes pay for procedures more than for counseling. Thus, 10 minutes suturing a laceration are worth \$300, but 30 minutes counseling a patient to avoid violence is not reimbursed. In managed-care settings, reimbursement is frequently capitated, so spending time preventing disease is worthwhile, because it prevents future disability and office visits.

Some interventions are not advised because they are so costly that any benefit would not be worthwhile; e.g., spending \$1 million to extend someone's life by 2 weeks.

Costs Versus Charges

What a laboratory or a hospital charges for a test may bear little relationship to what it costs to perform the test. Sometimes, calculating cost-benefit ratios should use costs, other times charges.

When considering costs, one needs to recognize not only the cost of screening tests, but also the cost of tests done to evaluate abnormal results of the screening tests. Frequently, a screening test will turn up a minor abnormality of no clinical significance, but one has to prove its insignificance by performing additional tests. Sometimes the chain continues to an extreme conclusion,

such as the patient who comes to thoracotomy to prove that an incidental nodule found on screening chest x-ray was benign.

Screening has secondary costs as well, such as missed work and emotional turmoil, even after negative findings.

While it is easy to calculate the costs of a screening procedure, the benefits are more difficult to assess. Researchers have settled on the surrogate benefit of the year of life saved, so that interventions can be compared quantitatively: the cost per year of life saved by screening mammography is \$30,000, for example. The cost per quality-adjusted year of life is another measure. An individual might feel that one year of blindness is equivalent to only 2 months of normal life.

AUTHORITIES

Screening recommendations have been made by many organizations, including the U.S. Preventive Services Task Force (2), the Canadian Task Force on the Periodic Health Examination, the American College of Physicians, and the American Cancer Society (ACS).

Preventive recommendations of narrower scope have been made by innumerable organizations, including the American Medical Association (*Guide to Adolescent Preventive Services*), the American Academy of Pediatrics (*TIPP: The Injury Prevention Program*), the American Academy of Family Physicians (*Put Prevention into Practice*), and most other medical specialty societies.

Chapters 41 through 47 present screening, counseling, and immunization recommendations for specific age groups. The U.S. Preventive Services Task Force represents the most conservative (least aggressive) view of screening, while the ACS and relevant specialty societies (e.g., American College of Obstetricians and Gynecologists) generally recommend more aggressive screening schedules. Because the recommendations of the various groups differ, physicians are sometimes uncertain which to follow. The detailed original recommendations provide scientific evidence to support the advice, enabling the individual physician to determine which specific recommendation is most logical.

References

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2. Guide to clinical preventive services. 2nd ed. Report of the US Preventive Services Task Force. Baltimore: Williams & Wilkins, 1996.



Preoperative Clearance and Preparation

Bruce T. Vanderhoff

INTRODUCTION

Family physicians are commonly asked to evaluate their patients before surgery. One of the primary responsibilities of the family physician during this preoperative evaluation is to segregate patients at low risk for surgery from those at greater risk. After identifying those patients whose surgical risk is intermediate to high, the family physician must often arrange for further risk assessment, consult appropriate subspecialists and/or advise the surgical team regarding perioperative medical management. At times it may be necessary to advise the patient and the surgeon against proceeding with a particular surgery. The physician who approaches this evaluation in an orderly and reasoned fashion will be the most effective advocate for the patient throughout the perioperative period.

PREOPERATIVE LABORATORY TESTING

Preoperative tests should be selected based on a patient's specific risk factors, such as age and concomitant disease. Ordering a fixed battery of tests routinely and indiscriminately on all preoperative patients is clearly not appropriate. Most authors appear to agree that no preoperative tests are necessary for "healthy" adults under 40, while testing for those older than 40 should be based on age and individual health problems. Suggestions for preoperative testing based on the recommendations of several authors are summarized in Table 37.1 (1-6).

Table 37.1.
Recommendations for obtaining preoperative tests.

Test	Indications
Hemoglobin	Age > 40, major surgery, renal disease, anemia, bleeding disorders, anticoagulant use, hemorrhage, hematologic malignancy, radiation/chemotherapy, other diseases associated with anemia
White blood cell count	Fever, suspected infection, disease of the white blood cells, hypersplenism, aplastic anemia, radiation/chemotherapy, alcohol dependency
Platelet count	Suspected bleeding disorder, known platelet disorder, hematologic malignancy, radiation/chemotherapy, thrombosis, some anemias
Prothrombin time/partial thromboplastin time	Suspected bleeding disorder, anticoagulant use, hemorrhage, anemia, liver disease, malignancy, malabsorption and malnutrition, alcohol dependency
Electrolytes	Age > 60, diuretic use, renal disease, diabetes mellitus, alcohol dependency, digoxin use, corticosteroid use, major surgery, major organ system disease
Blood urea nitrogen/creatinine	Age > 50, otherwise as for electrolytes above
Glucose	Diabetes mellitus, hypoglycemia, corticosteroid use, pancreatic disease, pituitary/hypothalamic/adrenal disease, alcohol dependency
Urinalysis	Age > 65, suspected urinary tract infection, renal disease
Albumin	Age > 65, suspected malnutrition, alcohol dependency
Chest x-ray	Age > 60, pulmonary disease, cardiac disease, malignancy, high risk for tuberculosis, alcohol dependency

Modified from Table 2 in Kaplan EB, Sheiner LB, Boeckmann AJ, et al. The usefulness of preoperative laboratory screening. *JAMA* 1985;253(24):3576–3581, and Table 3-2 in Lubin MF. Preoperative testing. In: Lubin MF, Walker HK, Smith RB, eds. *Medical management of the surgical patient*. 3rd ed. Philadelphia: Lippincott-Raven, 1995:35–39.

Preoperative Electrocardiography

Weitz has presented reasonable recommendations for when to obtain preoperative electrocardiograms (ECGs) (7). They include patients with significant risk factors for cardiac disease, such as hypertension and diabetes; patients with peripheral atherosclerosis, who frequently have occult coronary artery disease; patients with electrolyte disturbances, and patients taking non-cardiac medicines that can affect the cardiovascular system, such as tricyclic antidepressants, phenothiazines, and anthracycline chemotherapeutic agents. Weitz also suggests that preoperative ECGs be performed on patients with histories of cardiac dysrhythmias and in those anticipating higher risk surgery, such as thoracic, abdominal or emergency surgery; and patients at risk for heart disease (i.e., men older than 35 to 40 years and women older than 50 years) (7). It also seems reasonable to obtain pre-operative ECGs in patients with known alcohol dependency (8) (Table 37.2).

ASSESSMENT OF PERIOPERATIVE RISK AND PREPARATION

Nutritional Assessment

The nutritional status of patients plays a crucial role in their recovery from surgery as malnutrition is a recognized risk factor for postoperative morbidity and mortality. One must be alert to such factors as changes in appetite, dietary habits, vomiting, diarrhea

Table 37.2.
Recommendations for obtaining preoperative ECGs.

Men > 35 or 40
Women > 50
Alcohol dependency
Pulmonary disease
Cardiac disease
Significant risk factors for cardiac disease (e.g., diabetes, hypertension)
Peripheral atherosclerosis
Electrolyte disturbances
Noncardiac medicines affecting cardiovascular system (tricyclic antidepressants, phenothiazines, anthracycline chemotherapeutic agents)
History of cardiac arrhythmias
Higher risk surgeries (thoracic, abdominal, emergency)

and weight loss, particularly of more than 10% over the preceding 6 months. Pertinent gastrointestinal surgical procedures, such as gastric or bowel resections, should also be noted. Minimum physical examination criteria should include an accurate weight, a notation of general appearance and careful observations of signs of wasting or malnutrition (6, 9). The laboratory assessment of nutrition applies most to patients suspected of being malnourished based on history or physical findings. This includes measurements of serum visceral proteins (indicators of protein stores), such as albumin, prealbumin, and transferrin, and a determination of the total lymphocyte count. These are particularly helpful in assessing patients with hypoalbuminemic malnutrition because weight loss is often absent in this form of malnutrition despite a severe depletion of visceral protein stores. Because these serum studies can be affected by intravenous fluid administration and physical stress, it is best to obtain them prior to surgery. Guidelines for estimating the severity of malnutrition based on these parameters are outlined in Table 37.3 (10).

Assessing the Need for Nutritional Supplementation

Once a patient is noted to be malnourished or at risk for malnutrition, nutritional supplementation should be considered. Prior to initiating any nutritional therapy, the patient's oral calorie and protein intake should be quantified by the hospital dietitian, generally 35 kcal/kg, 20% of which should be protein. This assessment will identify many patients whose oral intake is good, but

Table 37.3.
Assessing malnutrition.

	Severity of Malnutrition		
	Mild	Moderate	Severe
Weight loss (%)	<10	10–20	>20
Albumin (g/dL)	<3.5	<3.0	<2.0
Transferrin (mg/dL)	<220	<170	<100
Prealbumin (mg/dL)	<17	<12	<7
Total loymphocyte count (cells/mm ³)	<2000	<1500	<1000

Modified from Table 2-2 in Ansley JD. Nutrition. In: Lubin MF, Walker HK, Smith RB, eds. Medical management of the surgical patient. 3rd ed. Philadelphia: Lippincott-Raven, 1995:21–31.

whose nutrient and calorie intake is inadequate. A variety of available oral supplements are usually appropriate for these patients. Even in patients unable to maintain adequate oral intake, nutritional support should be given through the gastrointestinal tract to the extent possible. Enteral perioperative nutritional support helps to maintain normal gastrointestinal structure and function, and is easier, safer, and less expensive than parenteral nutrition. When adequate oral feeding or supplementation is not possible, enteral tube feeding should be considered, while percutaneous gastrostomy or gastrojejunostomy may be useful if prolonged enteral feeding is anticipated. Consultation with a dietitian familiar with the many special nutritional support formulas now available will increase the likelihood that each patient's unique nutritional needs are met (9, 10). Some authors advocate the administration of total parenteral nutrition (TPN) for severely malnourished patients during the week prior to surgery. However, the evidence supporting such an approach is inconclusive (9, 10). Patients with good nutritional status and those with only mild malnutrition may require special nutritional support if adequate oral intake will not resume within 7 days of surgery, while those with moderate malnutrition may benefit from such support if oral intake will be delayed 3 to 5 days (10, 11). Emergent surgical intervention should not be delayed to permit an arbitrary period of parenteral nutritional repletion, regardless of the patient's degree of malnutrition. Such a delay is likely only to worsen the patient's condition and eventual response to surgery (9).

Assessing Cardiac Risk

As with preoperative laboratory testing, controversy surrounds the question of what constitutes an appropriate preoperative cardiac risk assessment. One-third of patients having surgery are likely to have coronary artery disease (12), and further risk is determined by what type of surgery is planned. Surgeries considered to be high risk for coronary events include vascular, thoracic, intraabdominal, and major orthopedic procedures, excluding, usually, total knee replacements (11, 13). In some cases, these procedures may pose an unacceptable risk when compared with other options, and further preoperative assessment becomes unnecessary. For example, debilitated patients with hip fractures survive longer and with fewer complications if managed without surgery rather than with surgery (11).

Risk Stratification

Many factors other than the type of surgical procedure have been suggested to increase the risk of perioperative cardiac complications. The first formal multifactorial assessment of surgical risk was introduced by Goldman and colleagues (14) and developed by others (15, 16). Detsky's modified risk index is reproduced in Table 37.4. Thus, index patients can be stratified into three groups by range of scores: 0–15, 15–30, >30. The majority of cardiac complications occur above a score of 16. The likelihood ratios for cardiac complications for these three groups have been reported to be 0.43, 3.38, and 10.60, respectively (11). While the predictive power of these indices appears to be low in low-risk patients (7, 11), such indices provide useful tools for the assessment of perioperative cardiac risk.

Table 37.4.
Modified multifactorial risk index.

	Points
Coronary artery disease	
Myocardial infarction within 6 months	10
Myocardial infarction more than 6 months	5
Canadian Cardiovascular Society angina	
Class III: (walking 1–2 level blocks or 1 flight of stairs)	10
Class IV: (with any activity)	20
Unstable angina within 6 months	10
Alveolar pulmonary edema	
Within 1 week	10
Ever	5
Valvular disease (suspect critical aortic stenosis)	20
Arrhythmias	
Rhythm other than sinus or sinus plus atrial premature beats on last preoperative ECG	5
More than five premature ventricular contractions at any time prior to surgery	5
Poor general medical status	5
Age over 70	5
Emergency operation	10

Detsky AS, Abrams HB, Forbath N, et al. Cardiac assessment for patients undergoing noncardiac surgery. *Arch Intern Med* 1986;146:2131–2134. (Copyright 1986, American Medical Association)

Cardiac Diagnostic Testing

For patients with good exercise tolerance and low cardiovascular surgical risk, no further cardiac testing is usually necessary (7, 17). In addition, clinically stable patients anticipating relatively safe procedures, such as prostatectomy and ophthalmic surgery, usually do not require further cardiac evaluation unless they are stratified as at high risk for cardiac complications. For surgeries with increasingly high risk, further noninvasive testing may be needed if the patient is determined to be of intermediate to high risk, or if there is significant clinical suspicion of valvular or ischemic disease (11, 18). Many diagnostic modalities are now available for these evaluations, including ambulatory electrocardiography, which may reveal dysrhythmias, silent ischemia and heart block; radionuclide ventriculography to evaluate ejection fraction and wall motion; echocardiography to evaluate valvular function; and exercise or pharmacologic stress testing, which may be combined with nuclear imaging or echocardiography in the evaluation of ischemic disease. These tests are also expensive and should, therefore, be ordered rationally and prudently. The cost of obtaining a stress-imaging evaluation on all patients stratified as intermediate to high risk (assuming a charge of \$1000 per test) could be \$10 billion annually in this nation (12). Goldman has remarked that preoperative noninvasive cardiac testing applies to patients at significant risk for coronary artery disease, and is not warranted for patients who have no history of symptomatic cardiac disease and thus less than a 1% risk of cardiac death (19). Unfortunately, the best diagnostic strategy for assessing patients' preoperative cardiac risk remains controversial.

Special Populations

Angina. Patients who have chronic stable angina as their only risk factor and are physically active have a low risk for cardiac complications during noncardiac surgery. Unstable angina, however, represents a significant risk factor for perioperative cardiac complications, and in patients with classic anginal symptoms, the likelihood of coronary artery disease and myocardium at risk is very great. Thus, in patients with unstable angina, surgery should be delayed, if at all possible (20, 21), in order to optimize the antianginal regimen and to perform coronary arteriography if indicated.

Coronary revascularizations, indicated by coronary arteriography, should be accomplished before elective noncardiac surgery. If, however, the anticipated noncardiac surgery is essential and cannot be delayed, the use of parenteral β -blockers should be considered to reduce myocardial oxygen demand during the perioperative period. Invasive hemodynamic monitoring may also be useful (20, 22).

Antianginal medications are continued during the perioperative period. Previously prescribed beta-blockers should be continued up to the time of surgery and a long-acting agent such as atenolol should be considered on the morning of surgery. Oral β -blocker therapy should be resumed as soon as possible after surgery. If postoperative oral intake is delayed more than 24 hours, an intravenous agent such as propranolol should be administered. Patients maintained on calcium channel antagonists as outpatients are also given a long-acting agent on the morning of surgery and oral therapy resumed as soon as possible postoperatively. In patients unable to resume oral intake within 24 hours after surgery, topical or intravenous nitrates are generally substituted for the oral calcium channel blocker. This is because the calcium channel antagonists that are available for intravenous administration, verapamil and diltiazem, exert a primarily antiarrhythmic effect rather than an antianginal effect when given via this route (20).

Myocardial Infarction. Many studies have demonstrated that patients who have had a myocardial infarction are at increased risk for reinfarction and death related to noncardiac surgery. In recent years the rate of myocardial reinfarction after noncardiac surgery has declined substantially, but it remains highest in patients on whom surgery is performed less than 3 months after an initial myocardial infarction (18). Surgery performed within 3 months of a myocardial infarction is associated with an 8% to 30% risk of recurrent infarction or death perioperatively. If surgery is performed more than 6 months after myocardial infarction, that risk falls to 3.5% to 5% (11). Based on the foregoing information, purely elective surgery should be delayed until 6 months after myocardial infarction. Semielective surgery, particularly surgery such as tumor resection whose delay could be substantially detrimental to the patient, can probably be performed sooner provided the patient is otherwise at low risk. In higher risk patients coronary arteriography and revascularization

should be considered before semielective surgery is performed. Finally, emergency surgery should proceed when necessary and aggressive hemodynamic monitoring be employed (22).

Hypertension. It is common for hypertensives to have poor control of their disease at the time of the preoperative evaluation. Poorly controlled hypertension during the perioperative period is associated with an increased risk of cardiac complications (21). However, there is no benefit in postponing elective surgery to achieve better control in patients with stable hypertension and diastolic blood pressures of 110 mm Hg or less. Moreover, perioperative hypertension will occur in about 25% of patients with a history of hypertension, regardless of the level of preoperative control (22, 23). Patients maintained on an antihypertensive regimen prior to surgery should, in most cases, continue that regimen up to and including the morning of surgery. Diuretics are an exception due to the unique problems they present in the perioperative period. The hypokalemia that can be induced may stimulate cardiac dysrhythmias, particularly when coupled with intraoperative hypoxia. Hypokalemia associated with diuretic use should be repleted prior to surgery. Diuretics may also produce volume depletion, increasing the likelihood of anesthesia-related hypotension. Thus, diuretics should generally be discontinued at least 1 day before surgery.

Oral antihypertensive regimen should be resumed as soon as possible after surgery. If resumption of oral therapy must be delayed, alternative therapy or routes of delivery should be considered. Discontinuation of methyldopa can be associated with a withdrawal syndrome that includes rebound hypertension. If oral therapy is not possible, this medication can be given intravenously. Clonidine is likewise associated with a withdrawal syndrome when discontinued abruptly, but this occurs rarely when the dose is less than 1.2 mg daily. This syndrome is aggravated by propranolol, which blocks the peripheral vasodilatory beta receptors, leaving the vasoconstricting alpha receptors unopposed, hence this agent should not be substituted. It is advisable, therefore, to switch the patient to the transdermal clonidine preparation well before surgery, as it requires 48 to 72 hours to achieve therapeutic drug levels. Alternatively, intramuscular clonidine can be used in doses that are about half the oral dose. Beta-blockers also should not be abruptly discontinued and may be given intravenously as discussed for patients with angina (22, 24). Discontinuation of the calcium channel blockers can be associated

with rebound hypertension as well. A long-acting agent should be given on the morning of surgery as described for patients with angina, but when oral therapy is delayed, intravenous therapy with diltiazem or nitroprusside should be considered. The angiotensin-converting enzyme (ACE) inhibitors, unlike many other antihypertensives, are not associated with a withdrawal syndrome (22). Fortunately, enalaprilat is available for intravenous administration when oral therapy is not practical (24). As with other antihypertensives, oral therapy should be resumed as soon as possible after surgery.

Congestive Heart Failure. Congestive heart failure can be associated with an increased risk of perioperative cardiac complications (25). Detsky's modified index (16) includes alveolar pulmonary edema within 1 week before noncardiac surgery and a history of pulmonary edema at any time before surgery (Table 37.4). Indeed, evidence of congestive heart failure during the preoperative physical examination conferred the greatest risk of perioperative cardiac death of all the variables assessed in the multifactorial study by Goldman (14, 18). Congestive heart failure poses the greatest risk if clinical signs of this condition are present during the week preceding surgery. Thus, surgery should be delayed, if possible, until at least 1 week after the patient's congestive heart failure is stabilized (25). To avoid volume depletion and the risk of hypotension associated with general or spinal anesthesia, preoperative diuresis should stabilize the patient's congestive heart failure without producing orthostatic hypotension (23). Finally, invasive hemodynamic monitoring may be advisable for patients with congestive heart failure and conditions such as significant left ventricular dysfunction; critical aortic stenosis; unstable angina; recent myocardial infarction, particularly if significant shifts in intravascular volume are anticipated; substantial changes in preload or afterload, and patients at risk for perioperative myocardial ischemia (25). Patients who suffer from chronic congestive heart failure but who are well-compensated preoperatively should have their maintenance therapy maintained (22, 25) while anticipating the foregoing possible perioperative complications of outpatient medical therapy. Thus, if changes in orthostatic blood pressure and pulse are preoperatively documented, intravascular volume should be repleted. Serum potassium and possibly magnesium levels should be determined and abnormalities corrected preoperatively in order to minimize the risk of

dysrhythmias in the perioperative period (25). Because digoxin use has been associated with perioperative bradydysrhythmias, this agent should not be *started* before surgery. Patients who receive chronic digoxin therapy preoperatively should continue receiving it in the perioperative period. However, serum levels should be checked and any necessary dosing modifications made. If there is a decline in renal function during the perioperative period, serial serum determinations may be advisable. Finally, digoxin should be administered intravenously to those receiving chronic therapy if the resumption of oral therapy is delayed postoperatively (25). As in hypertension, patients maintained on ACE inhibitors should continue these agents until the time of surgery, and oral administration should be resumed as soon as possible after surgery. If oral intake is delayed postoperatively, then enalaprilat can be administered intravenously.

Anticoagulation Therapy. Aspirin can be discontinued 1 week before surgery and resumed 48 hours after surgery. Ticlopidine, however, should be discontinued 2 weeks before surgery (24). A bleeding time may be used to document the dissipation of aspirin's or ticlopidine's effect. Patients with histories of atrial fibrillation, deep vein thrombosis, and cerebrovascular accidents are often maintained on chronic warfarin or aspirin therapy. For these conditions, warfarin should be discontinued 3 to 5 days prior to admission and therapy resumed 3 to 5 days after surgery (12,24). Most surgeries, with exceptions including ophthalmic and neurologic, can be performed once the prothrombin time is less than 14 seconds (INR 1.5). Aspirin can be discontinued 1 week before surgery and resumed 48 hours after surgery. A bleeding time may be used to document the dissipation of aspirin's effect (12).

Some patients maintained on warfarin are at higher risk for thromboembolism. Such patients include those with certain prosthetic valves, recent deep vein thrombosis, or pulmonary embolism (24). Valves that pose the greatest risk of thromboembolism include ball-cage or Lillehei-Kastor valves and mechanical prostheses in the tricuspid position (12). These patients should be admitted prior to surgery, warfarin discontinued the day of admission, and intravenous heparin started. Surgery should wait until there is no longer any discernible warfarin anticoagulant effect. Heparin should be stopped 6 hours before surgery, and surgery should proceed after an acceptable partial thromboplastin time has been documented. Heparin should then be restarted 12 to

24 hours after surgery and warfarin resumed within 5 days after surgery (12, 24).

Pulmonary Assessment

Perioperative Pulmonary Risks

Reported incidences of perioperative pulmonary complications vary greatly, from 9% to 76%. However, in all reports the incidence increases as the surgical field nears the diaphragm. The site of surgery is the most important risk factor for the development of perioperative pulmonary complications. Patients having upper abdominal surgeries, such as cholecystectomy, have a much higher incidence of pulmonary complications than those having lower abdominal operations. Research has suggested that other important nonpulmonary risk factors include the duration of the surgical procedure, and possibly age and obesity. Important pulmonary risk factors include long-term and active smoking, chronic phlegm production, wheezing, and abnormal respiratory function (26).

Pulmonary Function Testing

Select patients should be considered for preoperative pulmonary function tests (PFTs). These patients include those anticipating thoracic or upper abdominal surgery; with histories of heavy smoking and cough; over 70 years of age; those with obesity; and those with pulmonary disease (27). Patients who have normal pulmonary function tests, particularly those with spirometry demonstrating a forced expired volume in 1 second (FEV_1) greater than 2 L, should be considered surgical candidates. Results of PFTs that are indicative of a high perioperative risk for pulmonary complications include a forced vital capacity (FVC) of $\leq 50\%$ predicted, an $FEV_1 \leq 2$ L, a maximal voluntary ventilation (MVV) $\leq 50\%$ predicted or a diffusing capacity of the lung for carbon monoxide (DLCO) $\leq 40\%$ predicted. (26) These results may indicate the need to maximize the patient's pulmonary therapy before repeating the PFTs and/or that the patient is a poor candidate for the anticipated surgical procedure.

Pulmonary Resection

Patients anticipating pulmonary resection require special consideration. In most cases the patients who are considered for this surgery are elderly smokers seeking a cure for malignant disease.

Pulmonary evaluation in these patients is largely aimed at determining if the patient is optimized for surgery and whether the resection will be tolerated. Preoperative optimization of pulmonary therapy and smoking cessation may decrease the risk of perioperative pulmonary complications. The extent and location of resection is an important determinant of perioperative risk as well. Pneumonectomy, for example, has a higher mortality than lobectomy, and right pneumonectomy is associated with a higher mortality than left (28). Pulmonary function testing in these patients should include spirometry both before and after bronchodilator therapy, MVV, and DLCO. Patients with an $FEV_1 > 2$ L, $MVV > 50\%$ predicted and $DLCO > 60\%$ predicted are generally considered candidates for any form of pulmonary resection without further testing. Patients with an $FEV_1 > 2$ L, but an $MVV < 50\%$ predicted or $DLCO < 60\%$ predicted are considered to be high risk and should have exercise testing. Patients who are able to exercise to an oxygen consumption exceeding 20 mL/kg/min appear to be at very low risk while those with a maximum oxygen consumption less than 10 mL/kg/min appear to have very high risk related to thoracotomy (28). All patients with an $FEV_1 < 2$ L should undergo ventilation and perfusion scanning. Ventilation and perfusion scanning allow for an accurate prediction of postresection spirometric function when performed in conjunction with spirometry. In healthy individuals, ventilation and perfusion are well-matched and uniform by volume. However, patients with vascular invasion or postobstructive atelectasis may have large areas that are neither ventilated nor perfused. Ventilation and perfusion scanning allow for the calculation of the relative contribution to pulmonary function made by the areas of lung being considered for resection. The postoperative FEV_1 is equal to the preoperative FEV_1 times the fractional contribution of radioactivity from the nonresected lung. Therefore, a patient anticipating resection of the right lung with an FEV_1 of 1.5 L and perfusion scanning showing 30% flow to the right lung and 70% flow to the left lung would have a postoperative FEV_1 of 1.05 L, compared with the minimally acceptable FEV_1 of 800 mL, thus approving the patient as a candidate for the right pneumonectomy (28).

Perioperative Management of Diabetes Mellitus

During the perioperative period, patients with diabetes mellitus are subjected not only to the stress of surgery, but also to some pe-

riod of interrupted oral intake. This requires some adjustment in therapy even for patients whose diabetes is well-controlled prior to surgery. Oral agents should be discontinued prior to surgery. The short-acting sulfonylureas, such as glyburide and glipizide, can be stopped the night before surgery, while the long-acting sulfonylureas, such as chlorpropamide, should be stopped 48 to 72 hours before surgery (24). Metformin should also be discontinued before surgery because of the risks associated with its use in patients with hypoxia, dehydration, and acidosis. Even temporary reductions in renal function, such as those noted after angiography, can result in lactic acidosis in patients taking metformin. Thus, as there is little experience in this country with this drug during the perioperative period, it would be prudent to discontinue metformin at least 2 days before surgery just as one would before angiography (29, 30). After surgery, the patient's blood glucose should be monitored every 6 hours, and hyperglycemia should be treated with regular insulin according to a sliding scale. Sulfonylurea therapy can be restarted once the patient has resumed full oral intake. Resumption of metformin should wait until the patient has resumed normal oral intake, renal and hepatic function have normalized, and there is no longer a likelihood of hypoxia, dehydration, or acidosis. Patients maintained on insulin for control of their diabetes require different management in the perioperative period. Patients treated with ultralente insulin should be changed to NPH insulin 3 days before surgery, while patients treated with NPH or regular insulin should continue their usual therapy until the morning of surgery. On the morning of surgery, patients should receive one-half their usual dose of NPH or regular insulin. During the intraoperative and postoperative periods patients with insulin-dependent diabetes should receive a continuous intravenous infusion of 5% dextrose solution at a rate of 1 to 2 mL/kg/hr, and blood glucose should be assessed every 4 to 6 hours. Any hyperglycemia noted during this time should be treated with regular insulin according to a sliding scale. Once the patient has resumed full oral intake, resumption of scheduled insulin therapy should be considered (24).

Antibiotic Prophylaxis Against Endocarditis

Although it is not possible to accurately predict which patient will develop endocarditis with a given procedure, certain cardiac conditions and certain surgical procedures are known to be more

frequently associated with bacterial endocarditis. Based on this knowledge, the American Heart Association has recommended antibiotic prophylaxis for selected cardiac conditions and surgical procedures. These recommendations are summarized in Tables 37.5 and 37.6 (31).

Standard Prophylactic Regimens

Dental, Oral, or Upper Respiratory Tract Procedures. The recommended prophylactic regimen for patients undergoing dental, oral, or upper respiratory tract procedures is amoxicillin 3.0 g orally 1 hour before the procedure and 1.5 g 6 hours after the initial dose. Patients allergic to penicillin or amoxicillin may take either erythromycin, as the ethylsuccinate 800 mg, or the stearate 1.0 gm orally 2 hours before the procedure, then half the dose 6 hours after the initial dose, *or* clindamycin 300 mg orally 1 hour before the procedure and 150 mg after the initial dose. Patients unable to take oral medication should receive ampicillin 2.0 g

Table 37.5.
Cardiac conditions for which endocarditis prophylaxis is recommended.

-
- Prosthetic cardiac valves, including bioprosthetic and homograft valves
 - Previous bacterial endocarditis, even in the absence of heart disease
 - Most congenital malformations
 - Patients with isolated secundum atrial septal defect do not require prophylaxis
 - Patients who have surgical repair without residua beyond 6 months of secundum atrial septal defect, ventricular septal defect, or patent ductus arteriosus do not require prophylaxis
 - Rheumatic and other acquired valvular dysfunction, even after valvular surgery
 - Patients with previous rheumatic fever without valvular dysfunction do not require prophylaxis
 - Hypertrophic cardiomyopathy
 - Mitral valve prolapse with valvular regurgitation
 - Patients without regurgitation do not require prophylaxis, however, those with thickening and/or redundancy of the valve leaflets may be at increased risk for endocarditis, particularly males \geq 45 years old

Note: *Prophylaxis is not recommended for patients with previous coronary artery bypass graft surgery; physiologic, functional or innocent heart murmurs; previous Kawasaki disease without valvular dysfunction; or cardiac pacemakers and implanted defibrillators*

Adapted from Table 1 in Dajani AS, Bisno AL, Chung KJ, et al. Prevention of bacterial endocarditis, recommendations by the American Heart Association. JAMA 1990; 264(22): 2919–2922. (Copyright 1990, American Medical Association)

Table 37.6.**Surgeries for which endocarditis prophylaxis is recommended.**

-
- Dental procedures known to induce gingival or mucosal bleeding, including cleaning
 - Tonsillectomy and/or adenoidectomy
 - Surgery involving the intestinal or respiratory mucosa
 - Bronchoscopy with a rigid bronchoscope
 - Sclerotherapy for esophageal varices
 - Esophageal dilatation
 - Gallbladder surgery
 - Cystoscopy
 - Urethral dilatation
 - Urethral catheterization if a urinary tract infection is present
 - Urinary tract surgery if a urinary tract infection is present
 - Prostatic surgery
 - Incision and drainage of infected tissue
 - Vaginal hysterectomy
 - Vaginal delivery in the presence of infection

Note: *Prophylaxis is not recommended for tympanostomy tube insertion; endotracheal intubation; bronchoscopy with a flexible bronchoscope, with or without biopsy; cardiac catheterization; endoscopy with or without gastrointestinal biopsy; cesarean section; in the absence of infection for urethral catheterization, dilation and curettage, uncomplicated vaginal delivery, therapeutic abortion, sterilization procedures, or insertion or removal of intrauterine devices.*

Adapted from Table 2 in Dajani AS, Bisno AL, Chung KJ, et al. Prevention of bacterial endocarditis, recommendations by the American Heart Association. JAMA 1990; 264(22): 2919–2922. (Copyright 1990, American Medical Association)

intramuscularly or intravenously 30 minutes before surgery followed by ampicillin 1.0 g intramuscularly/intravenously or amoxicillin 1.5 g 6 hours after the initial dose. Penicillin-allergic patients should receive clindamycin 300 mg intravenously 30 minutes before surgery and 150 mg intravenously/orally 6 hours after the initial dose (31). Patients who are at particularly high risk for developing endocarditis include those with prosthetic heart valves, a past history of endocarditis, or surgically constructed systemic-pulmonary shunts or conduits. In the past, the American Heart Association had advised a more stringent prophylactic regimen for these patients. In the recent guidelines issued in 1990, however, it was recognized that there are “substantial logistic and financial barriers to the use of parenteral regimens” and that foreign experience with oral regimens in high-risk patients has not demonstrated prophylactic failures. Consequently, the standard prophylactic regimen was recommended even for high-risk pa-

tients. The more stringent regimen was included, however, for those clinicians who prefer to continue its use. It includes intravenous or intramuscular administration of ampicillin 2.0 g plus gentamicin 1.5 mg/kg (not exceeding 80 mg) 30 minutes before surgery followed either by repeat administration of this regimen in 8 hours or amoxicillin 1.5 g orally 6 hours after the initial dose. Penicillin-allergic patients can receive vancomycin 1.0 g intravenously over 1 hour beginning 1 hour before the procedure. No repeat dose of vancomycin is necessary (31).

Gastrointestinal and Genitourinary Procedures. The genitourinary tract is second only to the oral cavity as a portal of entry for bacteria producing endocarditis. The gastrointestinal tract is a less important portal of entry than either. Endocarditis following surgery to either the gastrointestinal or genitourinary tracts is usually the result of enterococci. Antibiotic prophylaxis is, therefore, directed at these bacteria. The standard recommended regimen of antibiotic prophylaxis for these procedures is ampicillin 2.0 g plus gentamicin 1.5 mg/kg (not exceeding 80 mg) intravenously/intramuscularly 30 minutes before the procedure followed by either repeating this regimen 8 hours after the initial dose or giving amoxicillin 1.5 g orally 6 hours after initial dosing. Penicillin-allergic patients can receive vancomycin 1.0 g intravenously over 1 hour plus gentamicin 1.5 mg/kg (not exceeding 80 mg) intravenously/intramuscularly 1 hour before the procedure. Gentamicin dosing may be repeated 8 hours after the initial dose (31).

Cardiac Surgery. Patients with cardiac conditions predisposing them to endocarditis (Table 38.5) are at risk when undergoing open heart surgery. In addition, patients receiving prosthetic heart valves, prosthetic intravascular materials, or prosthetic intracardiac materials are at risk for endocarditis. These patients should receive antibiotic prophylaxis. Unfortunately, no single antibiotic regimen is effective against all the organisms that most often cause endocarditis in these cases. Such organisms include *Staphylococcus aureus*, coagulase-negative staphylococci, diptheroids, streptococci, Gram-negative bacteria, and fungi.

It is recommended that prophylaxis at the time of cardiac surgery be primarily directed against staphylococci. First-generation cephalosporins are most commonly used. However, the appropriate antibiotic will depend on the antibiotic susceptibility patterns at the hospital where surgery is performed. For example,

vancomycin would be a better choice at a hospital with a high prevalence of infection caused by methicillin-resistant *S. aureus*. Prophylaxis with the chosen antibiotic should be started immediately before surgery, repeated as needed to maintain levels intraoperatively and discontinued within 24 hours postoperatively. In order to avoid late postoperative endocarditis, a preoperative dental evaluation is recommended with completion of treatment before surgery when possible (31).

Special Considerations. Patients who receive penicillin, for secondary prevention of rheumatic fever or other reasons, may have viridans streptococci in their oral cavities resistant to penicillin, amoxicillin, and ampicillin. These patients should receive erythromycin or another alternative regimen for endocarditis prophylaxis, rather than a penicillin. Finally, patients receiving heparin or warfarin should not receive intramuscular administration of prophylactic antibiotics. Intravenous or oral administration is preferred in these patients (31).

Prevention of Postoperative Thromboembolic Disease

Refer to Chapter 6.

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Obesity and Dyslipidemias

*Patrick O. Smith, Sara L. Noble,
and William G. Johnson*

OBESITY

The 1983 Metropolitan Life Insurance height/weight table defines obesity to be body weight 20% above ideal. Mild obesity is defined as 20% to 40% above ideal weight; moderate obesity is 40% to 100%; and severe obesity 100% above ideal weight.

Studies indicate that 30% to 35% of men and women in the United States are obese. The prevalence of obesity among lower income women is much higher than that among women in higher socioeconomic levels (1).

Obesity is an independent mortality risk factor often accompanied by other comorbid risk factors, all of which obesity further aggravates (e.g., hypertension, diabetes, osteoarthritis, cancer). As weight increases above ideal body weight, mortality risks increase significantly (2).

Individuals who are obese have a greater incidence of hypertension, diabetes, cancer (e.g., colon, rectal, gallbladder, breast, cervix, endometrium, uterus, and ovary), arthritis, coronary heart disease, gallbladder disease, hyperlipidemia, sleep apnea, and pulmonary dysfunction.

Etiology

Obesity is determined by biobehavioral factors whose interaction varies across individuals and is not fully understood. Twin and

adoption studies suggest that genetic factors account for a great amount of obesity. However, it remains unclear what components of obesity are inherited.

Behavioral Influences

Rate of energy intake does not explain obesity. Individuals who are in a "static phase" of obesity do not consume more calories than individuals who are nonobese. An energy intake difference, demonstrated by weight gain in adolescents and young adults, is referred to as the "dynamic phase," during which the caloric intake is increased.

At least 30% of obese individuals seeking treatment suffer from binge eating disorder. Individuals with binge eating disorder have more psychological disturbances, difficulty in losing weight, and maintenance of that loss.

Rates of energy expenditure are lower in obesity. Physical activity is lower in individuals who are obese when compared with nonobese counterparts. Inactivity is strongly associated with development of obesity in children, adolescents, and young adults.

Individuals who are obese do not experience any greater levels of psychological problems in comparison with the general population, but do take in more calories than nonobese people when exposed to anxiety-arousing circumstances. Also, individuals who are obese and are dieting are prone to higher levels of depression.

Treatment

Mild obesity warrants conservative methods such as cutting back on fat intake and beginning an exercise program. Self-help programs and support groups provide assistance. Those with moderate obesity should consider a professionally managed weight control program. Finally, more aggressive very low calorie diets (VLCD), pharmacotherapy, and direct invasive surgical techniques are available for the severe cases. Scare tactics have not been shown to be effective. Beyond patient education, the physician should reinforce the referral network by identifying a range of treatment services. Programs that are combined with cognitive behavioral therapies are generally more effective. Treatment outcomes vary considerably, and no single approach safely and reliably results in large and lasting weight loss. Obesity treat-

ment requires intense maintenance within the individual's genetic limitations (3).

Self-Help Programs

Overeaters Anonymous (OA) may be the best known self-help program. It is expense-free, is based on the Alcoholics Anonymous' (AA) 12-step program, and focuses on controlling addictive eating rather than weight loss per se. No empirical research has assessed the efficacy of this approach. Another popular self-help program is Take Off Pounds Sensibly (TOPS). TOPS uses a weekly group meeting format focusing on weight measurement with specific topic presentations. Volunteer leaders label members who have gained or lost the most weight in the last week. Research on this program suggests high attrition with modest weight loss (14.5 lbs.) at 19 months in treatment.

Commercial Programs

Probably the most well-known and representative program of this type is Weight Watchers International. Weight Watchers provides nutritional education, behavioral strategies related to eating and activity behaviors, and a social support network. Weight loss is the focus at weekly meetings. Research on commercial programs indicates high attrition, modest weight loss (11 to 22 lbs.), and a high incidence of weight regain.

Behavioral Therapy

Cognitive and behavioral techniques are used to change energy balance with expenditure exceeding intake. Most obesity treatment programs include common behavioral interventions (e.g., self-monitoring, stimulus control, contingency management, and topography modification) used in conjunction with cognitive restructuring, nutritional training, and exercise recommendations. This approach is usually couched within genetic limitations to assist in realistic goal setting. Behavior therapy interventions are most effective for patients in the mild to moderate range of obesity for weight loss up to a year. However, at 5-year follow-ups virtually all participants return to their original weight. Behavior therapy interventions are, however, effective in treating binge eating disorder, nutrition improvement, and in increasing physical activity.

Pharmacotherapy

When pharmacotherapy is employed, it should be part of a total treatment program that includes proper nutrition, exercise, and behavioral counseling. Pharmacotherapy, consisting of anorectic agents, can decrease appetite, increase energy expenditure, interfere with gut nutrient absorption, and influence fat metabolism. However, weight gain after drug termination is common if other interventions are not in place. Concerns exist for abuse potential of anorectics. Anorectic drugs act on the noradrenergic or serotonergic systems to decrease appetite. The noradrenergic agents are chemically related to amphetamine, except for mazindol. Schedule II drugs such as amphetamine, dexamphetamine, or phenmetrazine as treatment for obesity are illegal. Anorectic efficacy occurs within the first few weeks of therapy (i.e., weight loss from noradrenergic drugs = 0.51 lb/wk; serotonergic drugs = 0.55 lb/wk). Sustained drug use can lead to a weight loss plateau.

Noradrenergic Drugs. Schedule III drugs included are benzphetamine and phendimetrazine; Schedule IV drugs in this category are diethylpropion, mazindol, phentermine. Phenylpropanolamine is nonprescription. Side effects include nervousness, irritability, headache, insomnia, sweating, dry mouth, tachycardia, and hypertension. Tolerance occurs as manifested by weight loss plateau. Contraindications to use of noradrenergic drugs are coronary artery disease, glaucoma, hypertension, and hyperthyroidism.

Serotonergic Agents. This category includes fluoxetine and the Schedule IV drugs, fenfluramine and dexfenfluramine. Although not FDA approved for weight loss, studies of fluoxetine dosed at 60 mg/day have demonstrated weight loss. Fluoxetine's common side effects include gastrointestinal (GI) disturbances, sleep disturbances, nervousness, and headache. Fenfluramine, if stopped abruptly, can cause depression, as well as drowsiness, lethargy, and GI symptoms, as a general side effect. Dexfenfluramine is the first new prescription weight loss drug available in two decades. Dexfenfluramine side effects include asthenia, diarrhea, dry mouth, and somnolence, all of which are self-limiting and tend to resolve. Rare, but serious idiosyncratic primary pulmonary hypertension has occurred. Neurotoxicity in animals has occurred and is being investigated (4, 5).

Very Low Calorie Diets (VLCDs)

VLCDs contain less than 800 kcal/day in the form of a powder or solid protein formula. Treatment includes a medically supervised low calorie diet for 4 weeks followed by 12 to 16 weeks of VLCD. Solid foods are then reintroduced over 4 to 8 weeks. VLCDs should be reserved for patients at least 30% overweight who have failed to lose weight using more conservative approaches. Side effects include hair loss, chilly sensation, and skin thinning. VLCDs are contraindicated in lactating and pregnant women, children, elderly patients, or patients with cardiac dysrhythmia, unstable angina, hepatic or renal insufficiency, type I diabetes, or gout. There is impressive initial weight loss with VLCDs. However, long-term maintenance of the initial weight loss is rare.

Invasive Techniques

The primary form of invasive intervention is surgery. Mechanical interventions (e.g., jaw wiring, waistcord, and intragastric balloon) are used more rarely. Patient selection is crucial. Persons who are 100 pounds or 100% over ideal body weight, have a serious medical condition related to obesity, or have a history of multiple unsuccessful attempts to lose weight should be considered for surgical intervention. Surgical treatments available include bypass, gastric reduction, gastropplasties, and gastric banding procedures. At present, vertical-banded gastroplasty and gastric bypass are the two most common procedures. Gastric bypass circumvents a section of the stomach, while gastroplasty reduces stomach cavity size, restricting the amount of food that can be eaten at one episode.

DYSLIPIDEMIA

Dyslipidemia is a collection of lipid disorders in which lipid metabolism malfunctions. Cholesterol, triglycerides (T.G.), and phospholipids are the major plasma lipids. As weight increases with age, serum total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) increases 1 to 2 mg/dL per year in men from ages 20 to 40, 2 mg/dL per year in women from ages 40 to 60, and an average 18% during the perimenopausal period. Eight percent to nine percent of adults under the age of 35 have serum cholesterol of 240 mg/dL or higher, while nearly 25% of

men age 55 and approximately 40% of women over age 65 have serum cholesterol of 240 mg/dL or higher. For high-density lipoprotein cholesterol (HDL-C) values less than 35 mg/dL with desirable or borderline-high total cholesterol, prevalence is estimated to be 11% in men and 3% in women over age 20 (6). Dyslipidemia etiology is classified as primary, secondary, and dietary (Table 38.1). These causes should be screened for and treated.

Health Risks

Elevated serum cholesterol is an independent risk factor for coronary heart disease (CHD), the leading cause of death in the United States. CHD results in 490,000 deaths per year and significant morbidity related to nonfatal myocardial infarction (MI) and angina. For each 1% increase in TC, CHD risk increases by 3%. See Table 5.5 for relative importance of CHD risk factors.

Assessment and Measurement

The National Cholesterol Education's Panel (NCEP) recommends TC measurements for classification and follow-up as

Table 38.1.
Etiology of hyperlipoproteinemia.

Primary (genetic)	
	Common hypercholesterolemia
	Common dyslipidemias include: familial hypercholesterolemia, familial combined hyperlipidemia, polygenic hypercholesterolemia, familial hypoalphalipoproteinemia, familial defective apolipoprotein B-100, and familial dysbetalipoproteinemia
	Less common primary genetic hypercholesterolemias
Secondary	
	Diabetes Mellitus
	Hypothyroidism
	Multiple myeloma
	Nephrotic syndrome
	Pregnancy
	Systemic lupus erythematosus
	Drug-induced (alcohol, beta-blockers, corticosteroids, oral contraceptives, thiazide diuretics)
	Stress-induced
Dietary	
	High fat and cholesterol intake
	Obesity

Table 38.2.**Initial classification and recommended follow-up based on total cholesterol (TC).**

Classification	
<200	Desirable blood cholesterol
200–239	Borderline high blood cholesterol
>240	High blood cholesterol
Recommended follow-up (in mg/dL)	
TC <200 & HDL >35	Repeat in 5 years
TC=200–239	
Without CHD/2 CHD risk factors	Dietary information
CHD risk factors	Recheck annually
With definite CHD/or 2 CHD risk factors	Lipoprotein analysis & further action based on LDL cholesterol
Total cholesterol >240 mg/dL	Lipoprotein analysis & further action based on LDL cholesterol

Modified with permission from NCEP Guidelines (Adult Treatment II).

shown in Table 38.2. Screening should begin at age 20 and be repeated every 5 years according to NCEP (7). The American College of Physicians (ACP) recommends screening for men (ages 35 to 65) and women (ages 45 to 65). Screening is recommended outside of these guidelines when there is a family history of a lipoprotein disorder or at least two CHD risk factors are present (8). The Guide to Clinical Preventive Services, report of the U.S. Preventive Services Task Force, recommends that patients with TC values over 239 mg/dL and “borderline” patients with CHD or who have two or more risk factors should undergo a lipoprotein analysis. Further classification and treatment decisions are based upon the lipoprotein analysis (6). Only total and HDL cholesterol can be directly measured. The patient must be in a fasting state to obtain triglycerides (TG) and to calculate LDL cholesterol. The following formula can be used to calculate LDL cholesterol if TGs are less than 400 mg/dL: $LDL = TC \text{ minus } HDL \text{ minus } (TG/5)$. (TG/5 approximates the VLDL concentrations if $TG < 400 \text{ mg/dL}$ and patient is fasting.) Cholesterol measurements can be affected by stress, illness, posture, exercise, seasonal fluctuation, and laboratory error (9).

Treatment

Treatment planning should include risk assessment, at least two cholesterol measurements, and a third if the first two analyses have

a 16% difference. Cholesterol values >220 mg/dL or present atherosclerotic disease indicates drug therapy. Without these criteria, pharmacotherapy should be reserved following 6 months of lifestyle modification. Lifestyle modification includes adherence to a low fat/cholesterol diet, exercise, moderation of alcohol intake, and smoking cessation. The American Heart Association’s Step 1 and Step 2 diets are recommended (Table 38.3) The patient’s baseline LDL-C concentration, CHD risk factor profile, and history should determine initial treatment goals (Table 38.4). Dyslipidemia classification will guide the initial drug selection. The LDL-C drug effects should be the consideration in drug selection.

Pharmacotherapy

Bile Acid Sequestrants (BAS)

Cholestyramine (Questran) and colestipol (Colestid) have similar dose-related LDL-lowering efficacy and are not absorbed systemically. Most adverse effects are limited to the GI tract (ab-

Table 38.3.
American Heart Association’s step 1 and step 2 diets.

	AHA Step 1	AHA Step 2
Cholesterol (weight)	<300 mg	<200 mg
By percent of total calories:		
Fat	<30	<30
Saturated Fat	<10	<7
Protein	10–20	10–20
Carbohydrates	50–60	50–60

Modified with permission from NCEP Guidelines (Adult Treatment II).

Table 38.4.
Treatment guidelines based on LDL-cholesterol values.

Patient Category	Initiate Diet	LDL-C (mg/dL) Initiate Drug	Goal
No CHD			
<2 risk factors	≥160	≥190	<160
≥2 risk factors	≥130	≥160	<130
CHD	>100	≥130	≤100

Modified with permission from NCEP Guidelines (Adult Treatment II).

dominal bloating, belching, flatulence, heartburn, nausea, and constipation) and are addressed by gradual titration to full doses. BAS may decrease absorption of some oral medications (e.g., digoxin, iron, warfarin, thiazides, statins, and fat soluble vitamins). Patients should take medications 1 hour before or 4 hours after BASs. These drugs lower LDL-C by 15% to 30%, while only modestly raising HDL-C and perhaps raising T.G.

Dosing

Take BAS with fluid. The usual daily dosage of cholestyramine is 4 to 16 gm in divided doses; the maximum daily dosage is 32 gm. Colestipol's usual daily dosage is 5 to 20 gm in divided doses; the maximum daily dosage is 30 gm.

Niacin

Niacin lowers LDL-C by 10% to 25%, raises HDL-C by 15% to 35%, and lowers T.G. by 20% to 60%. It comes in immediate and sustained-release forms, though the sustained-release form is not recommended due to hepatotoxicity potential (10). Chronic liver disease and active peptic ulcer disease are absolute contraindications to niacin use. Diabetes mellitus, history of peptic ulcer disease, and gout are relative contraindications. The most common adverse effects are cutaneous flushing, pruritus, rash, and abdominal pain.

Monitoring

Baseline lipid profile, fasting glucose, liver function tests (LFTs), and serum uric acid values should be obtained with 3-month follow-up LFTs for the first year of immediate-release niacin. Discontinue niacin if LFTs are 3 times greater than normal. For patients with a history or symptoms of gout or hyperuricemia, a uric acid level should be obtained after maximizing dosage.

Dosing

Niacin should be initiated at a low dosage (i.e., 50 mg three times a day) and increased weekly incrementally by 50 to 100 mg to minimize skin flushing, itching, headache, or tingling due to niacin-induced vasodilation. An effective daily dosage of niacin is 1.5 to 3 gm; the maximum daily dosage is 6 gm. Assess lipid lev-

els after 4 weeks on 1.5 gm per day, and if necessary, increase dosage. Aspirin or NSAIDs should be taken 30 to 60 minutes before the morning dose for the first 2 weeks of therapy or when the daily dosage is increased to reduce vasodilatory side effects.

Statins (HMG-CoA Reductase Inhibitors)

This category has the strongest effect to lower LDL-C (25% to 45%), while raising HDL-C by 5% to 15% and lowering T.G. by 5% to 20%. Fluvastatin (Lescol), lovastatin (Mevacor), pravastatin (Pravachol), and simvastatin (Zocor) are HMG-CoA reductase inhibitors. With the exception of the fluvastatin, all statins cause a dose-related decrease in LDL-C. Statins are generally well-tolerated, and patients' noncompliance is rare. GI complaints and headache are the most commonly reported adverse effects. Changes in LFTs and myopathy development are the most important adverse effects. Cardiovascular morbidity and mortality have been reduced in statin treated patients (11, 12).

Monitoring

Assess baseline lipid profile, CK, LFTs, and renal function. Repeat lipid profile and LFTs at 6 and 12 weeks after drug therapy initiation or after an increase in dosage, and semiannually thereafter. Instruct patients to report weakness, tenderness, pain, or fever. CK should be repeated if patient reports muscle symptoms to confirm myopathy; if elevated, discontinue statin. Increased risk of myopathy and possibly rhabdomyolysis can occur when high-dose statins are combined with cyclosporin, erythromycin, gemfibrozil, or niacin.

Dosing

Initiate therapy with 20 mg of lovastatin (Mevacor), pravastatin (Pravachol), fluvastatin (Lescol), and 10 mg of simvastatin (Zocor). Take statins in the evening, with lovastatin being administered with the evening meal. Due to timing of cholesterol synthesis, a single evening dose is more effective than a single morning dose. Maximal effect is seen in approximately 4 weeks, and dosing adjustments should be made no more frequently than every 4 weeks. The maximum daily dosage of lovastatin is 80 mg; the maximum daily dosages of pravastatin, simvastatin, and fluvastatin is 40 mg.

Fibric Acids

This group has clinically favorable effects on HDL-C, raising levels 10% to 30%, and on T.G., lowering them 20% to 60%. LDL-C may be altered upward or downward unpredictably. Gemfibrozil (Lopid) is preferred over clofibrate (Atromid-S) because it does not adversely affect LDL-C as significantly. Side effects include GI complaints and gallstones. Used alone, gemfibrozil rarely causes myositis. Concurrent use with lovastatin and possibly other statins has resulted in rhabdomyolysis and acute renal failure. Gemfibrozil is contraindicated in patients with pre-existing gallbladder disease, biliary dysfunction, and hepatic or severe renal dysfunction. It should not be used in patients with a history of CHD (13, 14). Warfarin therapy should be re-evaluated for possible dosage adjustment with concomitant use of gemfibrozil.

Monitoring

Obtain baseline fasting serum triglycerides and cholesterol and monitor at 3- to 6-month intervals. If lipoprotein concentrations do not improve significantly after 3 months of treatment, gemfibrozil should be discontinued. LFTs and complete blood counts should be monitored periodically. Retest if elevated 3 times the upper limit of normal. If sustained increase occurs or if leukopenia or anemia develop, discontinue treatment.

Dosing

Gemfibrozil is taken 600 mg twice a day, 30 minutes before the morning and evening meal. No dosage titration or adjustment is needed.

Estrogen Replacement Therapy (ERT)

Effects of ERT, when employed after surgical or natural menopause, are comparable to those of niacin. ERT and hormone replacement therapy are discussed in Chapter 19.

Conclusion

Good evidence supports that lowering cholesterol results in decreased CHD risk. Screening of cholesterol is recommended to identify high-risk individuals who may benefit from diet or pharmacotherapy. Regular physical activity, reducing dietary fat, and

maintaining a healthy weight will help lower cholesterol in addition to providing other health benefits.

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Smoking Cessation

Edward T. Bope

SMOKING CESSATION

Nearly 0.5 million Americans die of tobacco-related health problems each year, a number nearly equal to the far leading cause of death, coronary artery disease (1). Many more suffer morbidity on a daily basis. Because it is a common and recurring problem in both ambulatory and inpatient medicine, every physician needs to develop an approach to the patient who uses tobacco. The impact of the first meeting with the patient and the multiple opportunities for follow-up enable effective family physician intervention. The family physician's influence on behavior change should not be underestimated. Even brief interventions have proved effective in helping patients identify and seek solutions to health problems.

Tobacco smoking has huge public-health implications, due not just to the health problems caused by nicotine and tobacco smoke on the smoking population. In addition, smoking affects 37% of nonsmokers with implications for their personal health (2) and the population at large who must pay the added health care costs. It is estimated that for the nation to go smoke-free would have ultimately an employment dampening effect of 0.2% for the tobacco-growing section of the country. Nearly twice the number of jobs lost in that region would be gained in the rest of the United States (3).

The introductory history should always include smoking and other tobacco use. Asking patients to complete a survey as part of registration helps to identify and quantify the smoking habit and relay the importance attached to smoking cessation. In addition, it may signal to patients that the physician has a special interest in smoking cessation and may have treatment options for them.

Having a smoke-free office is critical in setting the proper tone for positive health. Signs should be posted so that patients will recognize the commitment of the physician and the office staff. Many health educators advocate not using newspapers or magazines that advertise tobacco in waiting areas. In whatever way possible you need to inform patients that smoking is bad for their health and others and that your office will help them to stop.

Cigarette smoking is such an important adverse health factor that it should be listed on the chronic problem list on the patient chart so that it can be addressed. In many practices, smokers' charts are identified with a sticker or a large red mark alerting the clinician to look for smoking-related illness such as bronchitis, COPD, lung cancer, and cardiovascular disease. It may also be wise to identify the charts of smokers' children because they are more susceptible to ear and respiratory infections.

Each patient who is identified as a smoker must be confronted with the risks of smoking. Some smokers say that no one ever told them about the health consequences of smoking, and others say that their doctor never told them to quit. The benefits of smoking cessation are listed below and could be used as patient education.

Family physicians should commit to memory the sentence, "As your family doctor, I must advise you to stop smoking now." It should be used and documented at the initial visit and when appropriate at subsequent visits. Though it might be counterproductive to repeat at every subsequent visit, it would certainly be effective during a health assessment visit or when an episodic visit is tobacco-related. It is also a timely reminder at visits for an annual pap and pelvic because of the link between cervical cancer and tobacco use. An initial prenatal visit is an important time to ask about smoking, and there is an obligation to advise quitting based on its connection with low birth weight and preterm birth.

Smoking Cessation Benefits

Reduced Cancer Risk After Several Years of Cessation

Bladder cancer risk cut in half.

Cervical cancer risk reduced.

Throat, mouth, and esophageal cancer risk cut in half after 5 years.

Lung cancer risk cut in half after 10 years.

Pancreatic cancer risk reduced after 10 years.
Larynx cancer reduced.

Reduced Cardiovascular Disease After Several Years of Cessation

Coronary heart disease risk cut in half after 1 year.
Coronary heart disease risk is that of a nonsmoker after 15 years' cessation.
Peripheral vascular disease risk reduced.
Cerebrovascular accident reduced to that of nonsmoker after 5 to 15 years' cessation.

Other Benefits of Cessation

Risk of a low birth weight baby reduced to nonsmoker level if smoking is stopped before pregnancy or during the first trimester.
Risk of peptic ulcer disease reduced.
Risk of death from COPD reduced after long-term cessation.
Reduction in preterm birth.
Reduction in ear and upper respiratory infections in children of smokers (4).

Preparing the Patient for Smoking Cessation

Patients will arrive at the office visit at very different stages in regard to smoking cessation. Some patients are very comfortable with their smoking habit and have not actively considered stopping. With this group, you can only give them literature and let them know you are available if they become interested. Another larger group has anticipated quitting and may have tried on several occasions. These patients need a new "coach" and deserve a 5- or 10-minute intervention. They should be given literature and, if they are ready, be encouraged to set a stop date at this visit. If they are not ready to set a stop date, it is a good sign that a little more time is needed. A future appointment should be offered when they are ready to set a date for stopping. Some patients will come in ready to stop. They have moved to a point where they want to involve you for additional help, but their personal commitment is set and ready for implementation. Remember that

many people can quit “on their own” and will only need your support and some reinforcing literature. For this group, follow-up in the office or by telephone should be arranged to cement the support relationship. For those who have tried and failed to quit on multiple occasions, but are genuinely motivated to quit today, a more structured approach is needed. Such a patient has a stop date in mind that may be today, tomorrow, or even yesterday. That commitment should be reinforced. Assessment of the need for pharmacologic therapy is imperative.

Pharmacologic Intervention

Patients most likely to need pharmacologic help for cessation are those who have a strong physical addiction, which even they can identify, or those who have relapsed in the past due to nicotine withdrawal symptoms such as insomnia, irritability, hunger, anxiety, and difficulty concentrating. People are considered strongly addicted if they smoke more than one pack per day or have a cigarette within 30 minutes of getting out of bed. Those who have relapsed due to situations that made them want to smoke are more likely to benefit from behavioral therapy than from pharmacologic intervention because of their intermittent need for an alternative. They must come to grips with the urge to restart and develop a plan for subverting it. Obviously, they must have friends and family who are concerned about their restarting. Many smokers try to recruit these easy targets because it makes them feel less guilty about their destructive behavior. Warn your patients about these “friends.” In addition to behavioral therapy, these patients may also start nicotine replacement therapy.

There are three ways to replace nicotine while tapering it over several weeks. They are basically the “patch, nasal spray, and gum.” While some have used anxiolytics for a short term, and others have suggested clonidine as useful for female smokers, only nicotine products have been approved by the FDA. The gum and patch are now available without prescription, while the nasal spray remains by prescription only.

Using the Nicotine Patch

Advice: Patients should be advised that they must not smoke and use the patch *simultaneously*.

Dosage and administration: There are a number of manufacturers, all of which start with a dose that is weaned once or

twice over 10 to 16 weeks. Recent data indicates little benefit to the highest concentration patch and suggests that equal results can be gained using an intermediate dose patch. Because of the different dosages and schedules for reduction, it is best to check the manufacturer's information for dosage and usage. A decisional analysis study estimated costs per individual to be \$1210/year with a projected quit rate = 7.94% (5).

The patch is applied immediately after removal from its protective packet to a clean, dry, nonhairy surface once each day. The site should be rotated and not reused for 1 week to avoid contact irritation. Some systems are worn for a full 24 hours, while others are removed at bedtime. The dosage of the patch is then reduced per the manufacturer's schedule. It is best to make these changes during scheduled visits so that support and encouragement can be given.

Problems encountered: Many will note a mild itching or burning at the patch site that may last 15 to 60 minutes after application. Erythema with some edema is common, but true contact sensitization is rare. Other adverse reactions are diarrhea, dyspepsia, xerostomia, myalgia, arthralgia, abnormal dreams, insomnia, nervousness, and sweating. Reasons not to use the patch are hypersensitivity or allergy to nicotine or any part of the delivery system, a recent cardiac dysrhythmia, or infarction. In any patient, the risk of the patch should be weighed against the known risk of continued smoking.

Using Nicotine Gum

Advice: Nicotine gum is for use in patients who have stopped smoking. It should not be used to taper smoking or as an occasional cigarette substitute. Time should be spent encouraging the patient to learn to use and tolerate the gum. He/she should be encouraged to use the gum often enough to curb withdrawal symptoms. Acidic beverages such as coffee and soft drinks should be avoided.

Dosage and administration: Each piece of gum contains 2 mg of nicotine and is packaged in a box of 192 pieces. Patients should chew a piece of gum when they have the urge to smoke, with a maximum of 30 pieces per day. An alternative approach is to schedule a piece of gum every 30 to 60 minutes. The gum should be chewed in a slow, intermittent fashion until it softens and the tingling taste of nicotine is noted. The gum should then

be placed in contact with the oral mucosa and allowed to rest there (parked). It should be rechewed every few minutes to release more nicotine. A piece of gum will last about 30 minutes. The duration of therapy is very patient dependent. It probably should not exceed 6 months, but will likely last at least 3 months. Decision analysis suggests a lower cost per quality-of-life-year than with the nicotine patch. However, data are lacking for accurate comparison (5).

Problems encountered: Mouth and throat irritation, sore jaw muscles, gastric reflux, nausea, and palpitations. The gum should not be used in patients with a recent myocardial infarction, severe or changing angina, dysrhythmia, pregnancy, or breast feeding.

Using Nicotine Nasal Spray

Advice: This spray form has just been approved by the FDA and is now available under the name Nicotrol.

Dosage and administration: The pump bottle will deliver one puff containing 1 mg of nicotine. The dose is one puff in each nostril each hour. The product is then tapered as tolerated. It can be used for 3 to 6 months.

Problems encountered: Many patients will experience nasal or sinus irritation and so, therefore, would not be useful in patients with nasal and sinus conditions, allergies, or asthma. Warnings on the bottle will alert patients that 40 mg taken at once can be lethal.

The family physician is ideally suited to identify smokers and offer them treatment. Because of the continuous relationship of the physician and patient, there are multiple opportunities to intervene. Develop your own style for identifying, confronting, and helping your patients stop smoking. The rewards of success in smoking cessation are manifest to the patient, the doctor, and society.

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Exercise and Health

Mary Thoesen Coleman

One of the goals of *Healthy People 2000* (1) is to “increase to at least 30 percent the proportion of people aged 6 and older who engage regularly, preferably daily, in light to moderate physical activity for at least 30 minutes per day.” The U.S. population falls short of this goal, with only 22% of individuals meeting these standards; an additional 54% active to a lesser degree; and 24% reporting no leisure-time physical activity (2). Women are more sedentary than men; nonwhites more sedentary than whites; older less active than younger adults; and those with less income and less education more sedentary than those with more (1).

CURRENT RECOMMENDATIONS

The Centers for Disease Control and Prevention (CDC) and the American College of Sports Medicine (ACSM) recommend that every American spend a minimum of “30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week” (3).

Moderate-intensity physical activity is defined as physical activity performed at an intensity of 3 to 6 metabolic equivalents (METS). The MET is a measure of energy expended by (oxygen consumed) per unit of time: one MET corresponds to the approximate amount of oxygen consumed at rest, 3.5 ml/kg/min. An individual burns about 1 kcal/kg of body weight/hour/MET; thus, 60 kcal/hour/MET for a 60 kg person. For most healthy adults, physical activity corresponding to 3 to 6 METS equates to

brisk walking at 3 to 4 miles per hour and satisfies a definition of moderate physical activity. Other activities that typically consume 3 to 4 METS include playing tennis, slow stair climbing, cycling less than 10 miles per hour, swimming, and mowing the lawn with a power mower (Table 40.1). An individual who spends a minimum of 30 minutes of physical activity in moderate-intensity ex-

Table 40.1.

Examples of common physical activities for healthy U.S. adults by intensity of effort required in MET scores and kilocalories per minute. *

Light (<3.0 METs or <4 kcal·min ⁻¹)	Moderate (3.0 – 6.0 METs or 4 – 7 kcal·min ⁻¹)	Hard/Vigorous (>6.0 METs or >7 kcal·min ⁻¹)
Walking, slowly (strolling) (1–2 mph)	Walking, briskly (3–4 mph)	Walking, briskly uphill or with a load
Cycling, stationary (<50 W)	Cycling for pleasure or transportation (≤ 10 mph)	Cycling, fast or racing (>10 mph)
Swimming, slow treading	Swimming, moderate effort	Swimming, fast treading or crawl
Conditioning exercise, light stretching	Conditioning exercise, general calisthenics	Conditioning exercise, stair ergometer, ski machine
...	Racket sports, table tennis	Racket sports, singles tennis, racketball
Golf, power cart	Golf, pulling cart or carrying clubs	...
Bowling
Fishing, sitting	Fishing, standing/ casting	Fishing in stream
Boating, power	Canoeing, leisurely (2.0 – 3.9 mph)	Canoeing, rapidly (≥ 4 mph)
Home care, carpet sweeping	Home care, general cleaning	Moving furniture
Home repair, carpentry	Home repair, painting	...
Mowing lawn, riding mower	Mowing lawn, power mower	Mowing lawn, hand mower

*Pate RR, Pratt M, Blair SN, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. JAMA 1995;273(5):404.

ercise could expect to burn between 120 and 210 kcal. Another definition of moderate physical activity is that which produces about 70% of predicted maximum pulse rate (220 minus age).

By another estimate, somewhat more generous, the number of calories burned in walking a mile can be estimated by multiplying 0.67 times an individual's weight (4). For a 150-pound person, that is computed at about 100 calories per mile. While a few assumptions, e.g., that calories expended are proportional to oxygen consumed, which is proportional to the rate of blood flow, which is proportional to the pulse rate, the caloric value of other exercise can be estimated from pulse rate as follows:

$$\frac{\text{Calories expended other exercise for } x \text{ min}}{\text{Calories expended walking } x \text{ minutes}} = \frac{\text{Pulse rate other exercise for } x \text{ min}}{\text{Pulse rate walking}} \quad (5)$$

Figure 40.1 illustrates how calories for any pulse raising activity can be derived by developing the foregoing assumptions and formula. Thus, if a 150-pound person expends 100 calories walking one mile and maintains a pulse of 90 while walking at 3 mph (requiring 20 minutes to walk the mile), he or she may estimate calories burned in an activity sufficiently vigorous to raise the pulse to an average of 135/min for a total of 40 minutes, as calories expended in that activity = $100 \times 40/20 \times 135/90$ (ratio of vigor of exercise: vigor while walking) = 300 calories.

Individuals may achieve the recommended level of physical activity by summing minutes of activity participation throughout the day. These recommendations stress the goal of overall health

DERIVATION OF THE CALORIES EXPENDED IN A GIVEN PULSE RAISING ACTIVITY:

$$C_x = C_w \times P_x/P_w \times T_x/T_w$$

Where C_x = calories consumed in pulse raising exercise; C_w = calories consumed in locomotion one mile at any pace (weight in pounds \times .67); P_x = average pulse during that exercise; P_w = pulse while walking one mile at a steady pace, e.g., 3 mph; T_x = time exercised in minutes; T_w = time required to walk one mile while maintaining pulse P_w .

Figure 40.1. By David R. Rudy, MD, MPH, Department of Family Medicine, The Ohio State University, 1996.

fitness by daily participation in moderate physical activity but do not supplant earlier exercise guidelines geared toward achieving cardiovascular fitness: 20 to 60 minutes of sustained physical activity at 60% to 90% of maximum heart rate (220 minus age in years) three or more times a week.

BENEFITS OF EXERCISE

General Benefits

Regular exercise at a moderate level of intensity provides many health-related benefits. In both men and women, physical activity reduces the risk of *all-cause* mortality. It can also reduce stress and elevate mood, assist in weight control, and enhance ability to perform activities of daily living. Benefits such as stress reduction, mood elevation, and weight control may take place as soon as the individual begins exercising. Improvement in muscle strength may occur after 2 to 3 weeks of a regular program; cardiorespiratory improvement, as noted by a decrease in resting heart rate, quicker return of heart rate to baseline after physical activity, and ability to endure exercise longer or at a greater intensity without fatigue, may take 4 to 6 weeks. Some studies indicate cognitive processes are also improved (6).

Disease-Specific Benefits

The risk of developing coronary artery disease doubles in physically inactive individuals (7), a degree of risk similar to that of other risk factors (smoking, 2.5; hypertension, 2.1; and hypercholesterolemia, 2.4), but the prevalence of sedentary behavior in individuals (58%) is much higher than is smoking (25%), hypertension (30%), or elevated cholesterol (30%) (8).

Physical activity not only can reduce the risk of development of coronary heart disease; it can also reduce the incidence of cardiac arrest (9). In one study, Harvard alumni aged 70 to 84 who expended greater than 2000 kilocalories per week in exercise programs had half the all-cause death rate of age-matched alumni (10).

Both the development and management of hypertension are affected by exercise. Sedentary Harvard graduates were 35% more likely to develop hypertension than graduates who exercised vigorously for several hours each week (11). Less fit individuals, as assessed by treadmill testing, have 1.5 times the risk of

developing hypertension. Both mild-to-moderate and severe hypertension can be improved through a regimen of regular aerobic exercise. The mechanisms remain unclear, but may be related to insulin resistance and the pathogenesis of hypertension. In a study of the effects of regular exercise on blood pressure in African-American men, insulin levels, though not statistically different, were 33% lower than those at baseline in the exercise group and only 9% lower than baseline in the no-exercise group (10). Decreased catecholamine may also be involved (12).

Exercise favorably affects lipid profiles. Middle-aged men who exercised three times weekly for 20 weeks increased HDL cholesterol by 17% (13). Total cholesterol is lowered by exercise, even in patients who do not experience a change in weight (14).

Exercise positively improves glucose tolerance in noninsulin-dependent diabetes by decreasing insulin resistance, decreasing hepatic glucose production, by increasing the number of muscle cells, which use more glucose per pound than fat cells do (15), effects which may be due to weight reduction (see Chapter 31).

Sedentary individuals have lower bone mineral content, and weight-bearing exercise promotes an increase in bone mineral density (16). Lumbar bone mineral content increases in postmenopausal women after 9 months of exercising but decreases 13 months after cessation of exercise (17).

Regular exercise can increase exercise duration and distance in individuals with peripheral vascular disease (18) (see Chapter 6). Those with chronic obstructive pulmonary disease who exercise regularly can reduce minute ventilation and decrease carbon dioxide production (19). They also feel better and are able to walk greater distances.

A regular exercise program benefits people with arthritis in terms of reduced sick leave and hospital days and less swelling and pain. Active adults have less low back pain (20). Scores on mood questionnaires improved by participation in physical activity (21).

EXERCISE IN CHILDREN

Childhood physical activity patterns influence adult lifestyle habits. School-age children should participate in a minimum of 20 to 30 minutes of vigorous activity (involving large muscle groups in dynamic movement at 60% maximum cardiopulmonary capacity) at least three times weekly; a level achieved by only half of children in grades five through 12 (22).

EXERCISE IN THE ELDERLY

In addition to improved cardiopulmonary and muscular fitness in the elderly, exercise preserves functional ability. Regular exercise may delay the point at which an elderly person becomes too weak to lift him/herself from a chair or toilet seat, lacks flexibility in major joints needed for dressing or bathing, has insufficient oxygen transport to meet muscle needs during light aerobic work, or develops lack of motivation due to depression. Exercise programs may help avert hip fractures, cerebrovascular accidents, and complications of diabetes. Group participation may reap significant benefits in social support.

The ability of the body to transport oxygen from the air to the muscles reaches about 40 to 50 mL/min/kg body mass around age 20 and then declines at a rate of about 5 mL/min/kg body mass/decade regardless of activity level. However, regular exercise increases the peak oxygen transport by 5 to 10 mL/min/kg body mass at any given age and thus delays reaching the point of physical dependency.

RISKS OF EXERCISE

Prior to the initiation of an exercise program, risks for injury should be addressed. Attention should be paid to 1) neurological deficits that affect balance and coordination; 2) the presence of diabetes; and 3) medications that precipitate hypotension or dysrhythmias. During an acute illness or if there is significant or recent cardiovascular disease or symptoms, an exercise program is not recommended. Pregnant women in the third trimester or who are at high risk, should not begin a new exercise program. Most individuals, however, should err on the side of exercise. Even patients being treated for hypertension or hyperlipidemia on medications, if "healthy," can safely begin a moderately intense exercise program.

Any individual who experiences dizziness, shortness of breath, or chest pain during physical activity should stop further activity and seek evaluation. Sudden death is only rarely associated with vigorous activity: 1 per 360,000 hours of jogging (23). This corresponds roughly to a risk of sudden death of 1 in 1,400,000 per day for a person who jogs approximately 30 minutes per day, 7 days a week. Musculoskeletal injuries are more frequent with high-impact sports like jogging and less so for moderate-intensity exercise programs.

Most adults can begin a moderate-intensity exercise program without seeing a physician. Those who have cardiovascular, pulmonary, or metabolic disease, or symptoms suggestive of cardiovascular disease, e.g., ischemic chest pain, shortness of breath with exertion, dizziness or syncope, orthopnea or paroxysmal nocturnal dyspnea, ankle edema, palpitations of tachycardia, claudication, or heart murmur, should undergo an exercise tolerance test and/or further evaluation prior to moderate or vigorous exercise.

Adult men over 40, adult women over 50, and adults with more than one risk factor (hypertension, hyperlipidemia, smoking, positive family history for coronary disease, and/or diabetes) may safely begin a moderate-intensity exercise program. However, prior to beginning a *vigorous* exercise program (rhythmic, repetitive physical activity using large muscle groups at $>60\%$ maximum heart rate for age), individuals belonging to these groups should undergo an exercise tolerance test.

The level of activity may need to be adjusted if a person: 1) cannot carry on a conversation comfortably during the exercise; 2) remains fatigued at 1 hour after completion of the activity; 3) experiences dizziness, shortness of breath, or persistent headache; or 4) suffers an exercise-related injury or develops pain in his/her muscles or joints.

Inappropriate positioning while using home exercise equipment (e.g., stair climbers, cross-country ski machines, stationary cycles, and treadmills) increases risk of muscle and joint injury.

Benign Complications of Exercise in Athletes

The shift of splanchnic blood flow to skeletal muscle during exercise may precipitate symptoms of heartburn, belching, nausea, vomiting, cramping, urge to defecate, and diarrhea. These symptoms are rarely serious in an athlete and can be treated symptomatically with H₂-blockers, fasting prior to exercise, antacids, proper hydration, and loperamide. Exercise-caused reduction in renal blood flow may be responsible for postexercise proteinuria and hematuria. Unless they persist beyond 48 hours, neither requires intervention.

KEY COMPONENTS OF AN EXERCISE PROGRAM

Complete exercise programs address cardiorespiratory fitness, accounting for body composition, flexibility, muscular strength,

and muscular endurance. They are flexible and tailored to individuals' needs, reflecting their current health status, lifestyle, and goals.

They begin with a warm-up period followed by an activity phase and cool-down period.

WARM-UP PERIOD

The warm-up period typically lasts 5 to 10 minutes and consists of gentle stretching, light calisthenics, or low-intensity activity. As the heart rate gradually rises, both the body temperature and blood flow to muscles increase, permitting muscles and tendons to become more flexible, reducing the chance of muscle tears and pulls.

COOL-DOWN PERIOD

The 5- to 10-minute cool-down period consists of activities similar to those in the warm-up period and serves to avoid peripheral blood pooling in muscles from abrupt cessation of exercise. Symptoms such as vertigo, syncope, dysrhythmias, or nausea can result from sudden decreased blood supply to the brain, heart, and intestine. The cool-down period also helps return blood to the heart in sufficient quantities to clear lactic acid from the muscles.

ACTIVITY PHASE

The activity phase, directed at cardiorespiratory fitness, is the aerobic phase of the workout. (Aerobic metabolism uses oxygen to provide energy and is characteristic of sustained physical activity lasting 3 minutes or more.) Its four characteristics can be invoked by using the mnemonic FITT (Frequency, Intensity, Type, and Time). For sedentary individuals, an exercise program may begin with a frequency of once or twice a week and gradually increased. Individuals should be encouraged to develop exercise as a habit and to schedule a convenient time of day for it.

The intensity of exercise selected depends on age, risk factors, and goals. In light- to moderate-intensity exercise, the heart rate reaches less than 70% of maximum for age. An individual exercising at moderate intensity is usually able to comfortably carry on a conversation. Individuals who wish to compete usually require participation at a vigorous intensity.

To increase compliance, the type of physical activity should be enjoyable and compatible with the patient's lifestyle. For cardiorespiratory fitness, aerobic activities that are sustained and rhythmic using large muscle groups are necessary.

Thirty minutes of moderate-intensity exercise expending approximately 200 calories per day are necessary to reap health benefits. Sedentary people may start with a total of only 5 to 10 minutes per day. Some individuals may choose to exercise for two to three short periods throughout the day rather than in a single session. For weight reduction, longer sessions may be more efficient. Free weights, weight machines, and calisthenics two to three times a week increase muscular strength and endurance.

BARRIERS TO EXERCISE PARTICIPATION

Lack of time or motivation and inconvenience of group activity scheduling are cited as reasons for not exercising. Women often feel guilty and view such activity as taking time away from their families. The elderly, the socioeconomically disadvantaged, less educated, and those with disabilities each have special areas of difficulty in compliance.

INCREASING EXERCISE COMPLIANCE

Physicians can increase patient commitment to exercise by: 1) addressing exercise frequently at office visits; 2) being cognizant of and discussing feasible solutions to socioeconomic, life stage- and gender-specific barriers; 3) serving as role models; 4) engaging other health professionals, e.g., health educators, to assist in exercise prescription and monitoring, and 5) partnering with the public-health sector to offer exercise programs at convenient places—work sites, community centers, and parks near public transportation.

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Preventive Care and Triage of the Infant and Newborn

Bill G. Gegas

THE WELL BABY

The new baby provides the physician with numerous opportunities during the first year to assess, evaluate, and intervene if needed. The well baby should be examined approximately 1 to 2 weeks after discharge from the hospital, especially given the current trend for short-stay maternity care and early discharge. Other examinations should be scheduled at 2, 4, 6, 9 and 12 months of age. At each visit an accurate history should be taken from the parents to determine if any potential problems are developing. The diet should be assessed for appropriateness and developmental milestones checked. A careful physical examination should be done and any screening tests if indicated. Immunizations should be given at every opportunity and anticipatory guidance reviewed.

Points to Cover with the Parents at the First Opportunity

Umbilical Cord Care

Loss of water from Wharton jelly results in drying of the umbilical cord soon after birth. As the cord dries, it turns black and usually falls off within the first 2 weeks, although the time period varies from 3 to 45 days. The cord should be kept dry and clean by applying rubbing alcohol to the cord and base 3 or 4 times a

day. There is occasionally some bloody discharge from the navel just before and just after the cord separates. This usually resolves in a few days.

Bathing

Bathing every other day is usually adequate, and sponge baths are appropriate until the cord falls off. Bath water should be warm at all times, and a mild infant soap should be used. The infant should never be left unattended. When washing the anus and genitalia of girl infants the direction of wiping should always be from front to back to reduce the risk of urinary infections.

Circumcision

Controversy regarding neonatal circumcision persists. In 1975 and again in 1983, the American Academy of Pediatrics (AAP) stated, "There is no absolute indication for routine circumcision in the newborn." This position was changed in 1989 when the AAP stated that "newborn circumcision has potential medical benefits and advantages as well as disadvantages and risks" (1). In 1990, the American Academy of Family Physicians, while noting that the medical literature was conflicting, issued the following statement: "The decision to perform neonatal circumcision should be based on the informed consent of the parents and requires objective, factual counseling of parents by the family physician" (2). If done, circumcision is an elective surgical procedure that should be performed only on healthy infants. Circumcision has been shown to reduce the incidence of cancer of the penis and may result in a decreased incidence of urinary tract infections. Additional potential medical benefits include prevention of phimosis and paraphimosis. Circumcision is contraindicated if any penile abnormality is present, and appropriate urologic consultation should be obtained. If done, dorsal penile nerve block is effective in alleviating pain and is associated with a low rate of minor complications. Complications of the procedure itself are infrequent and usually consist of excessive bleeding, which is generally controlled with pressure. Infections may occur, but most are local. Sepsis is rare but is a reported cause of mortality. Other complications include the removal of too much foreskin or urethral injury. After circumcision the penis may be raw and red. The area should be cleaned with a gentle soap and water, and

petrolatum should be applied to keep the diaper from sticking. If the infant has not been circumcised, the foreskin should not be forcibly retracted.

Vaginal Discharge

Girl babies may have a whitish discharge and bleeding from the vagina. This is due to withdrawal of maternal hormones and is normal. No specific treatment is needed.

Sleep Position and Sudden Infant Death Syndrome (SIDS)

Sudden Infant Death Syndrome is the leading cause of death in infants 1 to 12 months of age. Despite years of study, no definite cause has been found. In June 1992, however, based on the evaluation of studies from other countries indicating an association between SIDS and the prone (stomach) sleeping position, the American Academy of Pediatrics recommended that healthy infants be positioned on their sides or backs (3). The Academy recognized the limitations of many of the studies but also noted a 50 percent or greater reduction in SIDS rates in all of the countries in which the use of the prone sleeping position was reduced. The opinion of most authorities is that physicians should advise parents to place their infants in the supine or side positions when putting them to bed.

Colic

The term colic is used to describe the prolonged, unexplained episodes of crying that occur in otherwise healthy infants. Colic is most commonly seen between 3 weeks and 3 months of age. Since the cause is unknown, no specific treatment has been shown to be of consistent benefit.

Neonatal Conjunctivitis

Neonatal conjunctivitis, or ophthalmia neonatorum, is inflammation of the conjunctiva of the newborn. Chemical irritation is the most common cause and due to the instillation of ophthalmic drops for ocular prophylaxis of gonococcal conjunctivitis. This irritation is usually apparent 24 to 48 hours after birth. Chlamydia conjunctivitis is the most common infectious cause and appears 5 to 10 days after birth. Bacterial infection due to gonococcus,

staphylococcus, and pneumococcus produces irritation in 2 to 5 days after birth, while the major viral cause, herpes simplex types 1 and 2, may present 2 weeks after delivery (4). The routine usage of 1% silver nitrate, erythromycin, or tetracycline drops or ointment into each eye at birth is recommended by the Centers for Disease Control and Prevention for prevention of neonatal gonococcal conjunctivitis. None of these prophylactic medications will prevent neonatal chlamydia conjunctivitis. Chlamydia conjunctivitis should be treated with erythromycin syrup, 50 mg/kg/d orally in four divided doses for 14 days. Herpes simplex infections should be treated with intravenous acyclovir and 1% trifluridine drops every 2 hours for 1 week.

Infant Feeding

Breast Feeding

Breast feeding offers numerous advantages during the first several months of life. It provides optimum nutrition for the normal infant. It stimulates the uterus to contract and return to normal size more quickly. The milk is readily available at a proper temperature with little risk of bacterial contamination. Allergic diseases are less common in breast-fed infants, and the presence of immunologic factors in breast milk including secretory IgA, lysozyme, and macrophages help to provide protection against gastrointestinal and upper respiratory infections (5). Breast feeding also promotes maternal-infant interaction and bonding.

Disadvantages include the difficulty in maintaining lactation and feeding after mothers return to work. It places the primary responsibility of nutrition on the mother and reduces paternal assistance. Proper use of a breast pump is often needed, and certain groups of women including minority, low-income, and young mothers have traditionally had low breast feeding rates. True contraindications to breast feeding are few and include tuberculosis in the mother and the use of illicit drugs. Prescribed drugs that can be dangerous to the infant through the mother's milk include lithium, antithyroid drugs, antimetabolites, and tetracycline.

The first feeding may occur in the delivery room if the mother and infant are stable. Most hospitals have lactation specialists or nurses whose primary role is to teach and help mothers develop the technique for feeding that works best for them.

Most infants will feed about every 2 to 3 hours and some will pass stools with each feed. Mothers must be reassured that this frequency of feeding and stooling does not represent either inadequate milk production or diarrhea. Breast milk is generally not in good supply for the first 4 to 5 days and does not reach a maximum amount until about 1 to 2 weeks. The milk flow will be greater if both breasts are suckled by a hungry infant, and most infants will obtain enough milk by suckling for approximately 15 minutes at each breast. Longer periods may cause excessive tenderness and pain in the nipples, and mothers can develop infection (mastitis) requiring antibiotics. Breast feeding may continue during treatment, but analgesics may also be needed.

Formula Feeding

Mothers who choose to formula feed also benefit from proper instruction and support from the physician regarding their decision. Although all commercial preparations use breast milk as their model, none reproduces the digestive qualities and immunologic properties of human milk. Even so, they can be the sole food source for the first 6 months of life. Formulas are available in ready-to-feed, liquid concentrate, and powder forms, and for the typical infant most available brands have no clear advantage over another. The two most common types of formula are cow's-milk-based (Enfamil, Similac, Gerber) and soy-based (Isomil, Nursoy), with protein hydrolysate formulas (Nutramigen, Alimentum) used in infants who cannot tolerate either. Cow's-milk-based is the preferred choice and should always be iron-fortified. Studies have shown that iron-fortified formulas are not associated with an increase in gastrointestinal problems, and that low-iron formulas are associated with iron deficiency. To ensure adequate iron for the infant, the American Academy of Pediatrics Committee on Nutrition has recommended that only iron-fortified formulas be used (6). Soy protein formulas are commonly used in cases of suspected intolerance to cow's-milk protein, although infants with true cow's-milk protein intolerance may also be unable to tolerate soy protein. In addition, their vitamin content is lower, and soy formulas should not be used in preterm infants. The AAP Committee on Nutrition has issued specific recommendations: Soy formulas should be used in families who choose not to consume animal protein. Soy formulas should be used in infants with galactosemia or primary lactose

intolerance. Soy formulas may be used temporarily in infants with secondary lactose intolerance (following gastroenteritis, for example). Soy formulas may be used in allergy-prone infants. The committee specifically states that soy formulas should not be used in the management of cow's-milk protein allergy or colic. Protein hydrolysate, or semielemental, formulas contain milk protein that is heated and enzymatically hydrolyzed, or predigested, to free amino acids and peptides of smaller lengths. These are also supplemented with selected amino acids, and most are lactose-free. These formulas are useful in infants with malabsorption syndromes such as short bowel syndrome, chronic diarrhea, and cystic fibrosis. In addition, infants who truly have intolerance to cow's milk and soy protein may benefit from this type. There is no evidence to support their role in the treatment of infantile colic.

When initiating feeding, expect the newborn to take approximately 0.5 to 1 ounce per feeding and increase to about 2 ounces per feeding by day three, with 6 to 8 feedings per 24 hours. After day three, the average term newborn takes in about 100 mL/kg/day of milk. Sterilizing bottles and nipples is a matter of debate. While some formula makers recommend sterilization, others argue that if the water is sanitized and bottles are prepared one at a time, sterilization is unnecessary. Unsanitized water such as well water should be boiled for 5 minutes before preparing the formula.

Vitamins

All necessary vitamins are included in formulas; therefore, supplements are not needed during the first 6 months of life. If solid foods are combined with formula after 6 months, then vitamin and mineral supplements are still unnecessary.

Fluoride

Because of the increasing incidence of dental fluorosis, routine fluoride supplementation is no longer recommended for infants under 6 months of age. The AAP Committee on Nutrition recommends fluoride supplementation in infants older than 6 months who rely on spring water and distilled water for the preparation of their formulas or drinks, as well as infants who rely primarily on ready-to-feed formulas that are made with water low in fluoride.

Solids

The timing of the introduction of solid foods is variable and dependent on each baby. Currently the AAP recommends solids be offered between 4 and 6 months. Cereals are usually tried first, followed by fruits and vegetables. Meats are generally offered last.

PREVENTIVE CARE IN THE FIRST YEAR

Periodic Visits and Health Screening

There is no scientific evidence that following preventive health care schedules or recommendations reduces childhood morbidity or mortality, except for those on immunizations (4). Still, periodic visits enable the physician to provide instruction and guidance to the parents, as well as provide opportunities to detect disease early and initiate treatment.

Screening

Height and Weight

The height (or length if appropriate) and weight of all infants should be obtained at every visit and plotted on a growth chart or compared with tables of average measurements for gender to determine the need for further evaluation, treatment, or referral.

Metabolic Disorders

All states of the United States require newborn screens for phenylketonuria and hypothyroidism, and many states also require testing for various other disorders including galactosemia, maple syrup urine disease, homocystinuria, and biotinidase deficiency, as well as sickle cell disease and cystic fibrosis (7). The accuracy of these tests depends on the specimens being obtained at the appropriate times, and any positive screen should be followed by further testing specific to that disease, as well as immediate referral to appropriate consultants.

Phenylketonuria (PKU)

PKU is an inborn error of phenylalanine metabolism characterized by the absence of phenylalanine hydroxylase, which occurs in 1 of every 12,000 births in North America. Phenylalanine is

normally eliminated from the body by hydroxylation to tyrosine by phenylalanine hydroxylase. In the absence of this reaction phenylalanine accumulates and results in gait disorders, tremors, seizures, and eventually irreversible mental retardation. After drinking milk (the source of the phenylalanine) for at least 48 hours, serum levels begin to rise. Diagnosis depends on detecting elevated phenylalanine levels on dried-blood spot specimens obtained in the nursery. If infants are tested and discharged before 48 hours of age, repeat testing should be done by 2 weeks of age. Treatment involves restricting dietary phenylalanine intake. Since dietary therapy was introduced more than 95% of children with PKU have developed normal or near-normal intelligence.

Congenital Hypothyroidism

Congenital hypothyroidism occurs in approximately 1 of 4,000 infants born in the United States. Without treatment children develop irreversible mental retardation and growth failure. Studies have shown normal or near-normal intelligence in virtually all infants diagnosed and treated early in life. Screening with thyroid function tests performed on dried-blood specimens is therefore recommended for all newborns before discharge from the nursery or within the first week of life if born outside the hospital (more in Chapter 32).

Sickle Cell Disease

Sickle cell disease occurs in 1 in 375 African-Americans, 1 in 3,000 Native Americans, 1 in 20,000 Hispanics, and 1 in 60,000 whites (8). Children are normal at birth, and symptoms are rare before 3 to 4 months of age because high levels of fetal hemoglobin inhibit sickling. The infant may be functionally asplenic by this time, however, due to congestion of the spleen with sickled cells, which puts the child at great risk for infection with encapsulated bacteria, especially pneumococci. Hemoglobin electrophoresis can be performed from blood samples obtained in the nursery using the heel-stick method used for other screening tests. Infants with documented disease should be started on penicillin prophylaxis no later than 2 months of age. Recommendations differ, however, regarding whom to screen. Some authorities advocate universal screening, while others believe high-risk groups should be targeted (9).

Vision and Hearing Screening

The American Academy of Pediatrics and the American Academy of Ophthalmology each recommends that eye and vision screening be performed at birth and at approximately 6 months of age during the first year of life. The screening should consist of inspection of the eye for structural abnormalities and the presence of normal corneal light and red reflections (10). The National Institutes of Health and the Joint Committee on Infant Hearing recommend universal newborn hearing screening in order to identify hearing-impaired infants by 3 months of age and begin treatment by 6 months of age (11).

Blood Pressure

The AAP currently recommends against universal neonatal blood pressure screenings, and the Canadian Task Force found insufficient evidence to recommend for or against routine screening in individuals under 21 years of age. Accurate readings are difficult, and there are no studies showing that reducing blood pressure in children results in lowered blood pressure in adults.

Counseling for Injury Prevention

Auto Safety

Injury is the most common cause of death in childhood, exceeding those deaths from congenital malformations, cancer, pneumonia, meningitis, and heart disease combined, and almost half of these injury deaths are due to motor vehicle accidents. An unrestrained child can be injured in otherwise minor collisions. Child safety seats are required in all 50 states, as well as the District of Columbia and Puerto Rico, and should be used until the child weighs at least 40 lbs. Safety seats should face the rear window until the child weighs 18 to 20 lbs. and should never be placed in the front seat of a car with a passenger-side air bag.

Bicycle Helmets

The greatest incidence of head injuries occurs in children <1 year and >15 years of age. Bicycle helmets have been shown to reduce head injuries by at least 40%. All children should wear proper-fitting safety helmets when riding bicycles.

Other Safety Issues

Parents should be advised to install the proper number of smoke detectors in appropriate locations to reduce the risk of *fire injury*. Infants and toddlers should wear flame-resistant sleepwear.

Children can be protected from *scald burns* by setting hot water heaters at 120 to 130 degrees, and by installing antiscald devices on faucets.

Falls are common in childhood but few of these incidents lead to death or permanent injury. Still, these can be prevented by placing safety gates across stairways and window guards above the first floor.

As to *poison safety*, parents should be advised to keep a 1-ounce bottle of syrup of ipecac available and to use only after consulting with a poison control center or health-care professional. All medications and toxic substances should be out of reach and in child-resistant containers. The telephone number of the local poison control center should be displayed in a prominent area.

Cardiopulmonary Resuscitation (CPR)

The immediate initiation of CPR when needed, especially in children with water submersion injury, has been shown to improve outcome. Parents and caregivers should be advised to consider this training.

Household Tobacco Education

Parents should also be aware of the risks that passive or environmental smoking poses to their children. Passive smoking increases the risk of ear infections and middle ear effusions in children, and is associated with small but measureable reductions in lung function. It has also been shown to increase the severity of symptoms and attacks in children who are asthmatics. Environmental smoking is also linked to an increased risk of SIDS.

Dental Health

Parents should be advised against putting the infant or toddler to bed while sucking on a bottle. This activity is associated with an increase in enamel erosion in deciduous teeth known as "baby bottle syndrome." There are no guidelines for routine dental examinations during the first year of life.

Immunizations

Immunizations have been very successful in lowering the incidence of vaccine-preventable illnesses. A comparison of the total number of reported cases in the United States in 1994 and in the year preceding vaccination show a reduction of diphtheria from 9,493 in 1948 to 2, tetanus from 601 in 1948 to 51, polio from 18,308 in 1954 to zero, and measles from 481,530 in 1962 to 963 (12). Similar reductions are also seen with rubella, mumps, and *Haemophilus influenza* type b infections. Despite this success, however, studies have shown adequate immunization rates among 2-year-olds of only 55% to 88% (13).

Numerous misconceptions persist among parents and health-care professionals regarding both vaccine side effects and contraindications. For example, the only true contraindications to vaccination are 1) moderate to severe illness, 2) previous anaphylactic reaction to a specific vaccine, and 3) severe hypersensitivity to a vaccine component. In addition, live vaccines generally should not be given to pregnant or immunocompromised patients. See Appendix I for recommended immunization schedule.

DPT Vaccine

The whole-cell pertussis preparation, in addition to local side effects, is associated with more occurrences of fever, protracted crying, hypotonia, seizures, and severe neurologic illnesses at a rate of 6.8 per million doses (14). Despite this, the risk of serious neurologic dysfunction following pertussis disease is still substantially greater than from the vaccine. Acellular pertussis vaccines are available and, in addition to being comparable in immunogenicity to whole-cell preparations, are associated with fewer local and systemic side effects. The acellular form (DTaP) is licensed for use in the United States as the booster dose in children 15 months or older, but is likely to be approved for infants in the near future.

Oral Polio Vaccination (OPV)

Side effects to OPV are few, but approximately 1 out of 2.5 million doses of vaccine causes paralytic polio. Inactivated polio vaccine (IPV) has similar effectiveness but no reported serious adverse effects. The IPV requires injection. Current immunization schedules recommend 3 doses of OPV during the first year but consider IPV as an acceptable alternative.

Haemophilus influenza type b (Hib)

The incidence of invasive Hib disease, including meningitis and epiglottitis, fell almost 95% after its approval for usage in 1987. Side effects are mild and consist of tenderness, redness, irritability, and low-grade fever.

Hepatitis B Vaccine (HBV)

Universal vaccination of infants with a 3-dose regimen of hepatitis B vaccine is estimated to be >84% effective in preventing HBV infection, and approximately 80% effective in preventing the chronic carrier state. While there are case reports of nonfatal anaphylaxis from the vaccine, side effects are generally mild and consist of local tenderness, low-grade fevers, and similar benign symptoms.

THE SICK NEWBORN

Few situations in medicine are as challenging as the newborn who may have minimal symptoms and signs and yet be critically ill. Whether in the nursery or the office, the patient needs an attentive physician who can rapidly assess for serious conditions when nonspecific clinical signs are present.

Illness during the first few days of life will usually be due to congenital problems that manifest themselves such as heart or pulmonary defects, or infections such as Group B strep. The physician must also suspect the classic TORCH (Toxoplasmosis, "Other"—syphilis, hepatitis, enterovirus—Rubella, Cytomegalovirus, Herpes simplex) infection. Premature infants will have an increased risk of apnea and respiratory distress, as well as intracerebral hemorrhages and necrotizing enterocolitis. An infant who was previously well and becomes sick during the first month or so may have a condition that was missed at the initial exam, a delayed-onset infection, or even nosocomial-acquired infection such as *Staphylococcus*. Signs and symptoms of the ill newborn may be multiple or few. Clinical manifestations may be as subtle as poor feeding and irritability or as obvious as respiratory distress, cyanosis, and fever.

Evaluation of the Febrile Infant

Infants less than 1 year old are more susceptible to infection due to immunologic immaturity. An aggressive evaluation of fever is justified, as infants <2 years old with a rectal temperature over

39°C (102°F) and no other signs have a 3% to 5% incidence of occult bacteremia (15). A blood culture and total leukocyte count with differential should be considered in all cases. Approximately 65% of bacteremic children will have leukocyte counts >15,000. All infants younger than 3 months old should have a lumbar puncture regardless of whether irritability is present. A catheterized urine specimen should be obtained, and chest x-ray considered in any infant although the highest yield will be in babies who have respiratory symptoms. An evaluation and management algorithm for infants less than 3 years old is summarized in Figures 41.1 and 41.2.

Respiratory Distress

Respiratory distress is a common presentation for problems of both pulmonary and nonpulmonary etiology. Classic features include a

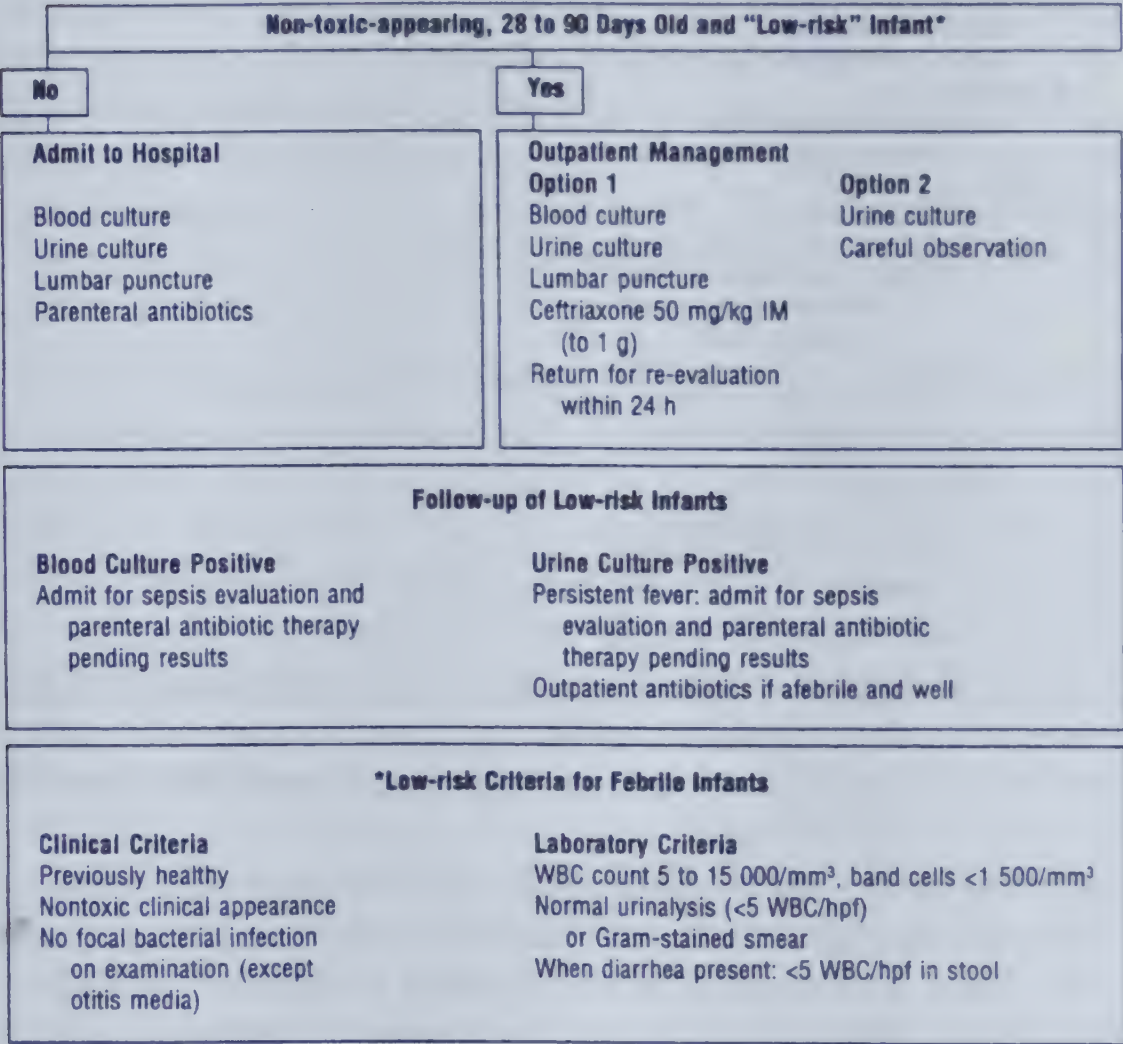


Figure 41.1. Algorithm for the management of a previously healthy infant 28 to 90 days of age with fever without source ≥ 38°C. (Reprinted with permission from the American Board of Family Practice. March-April 1995;8(2):116.)

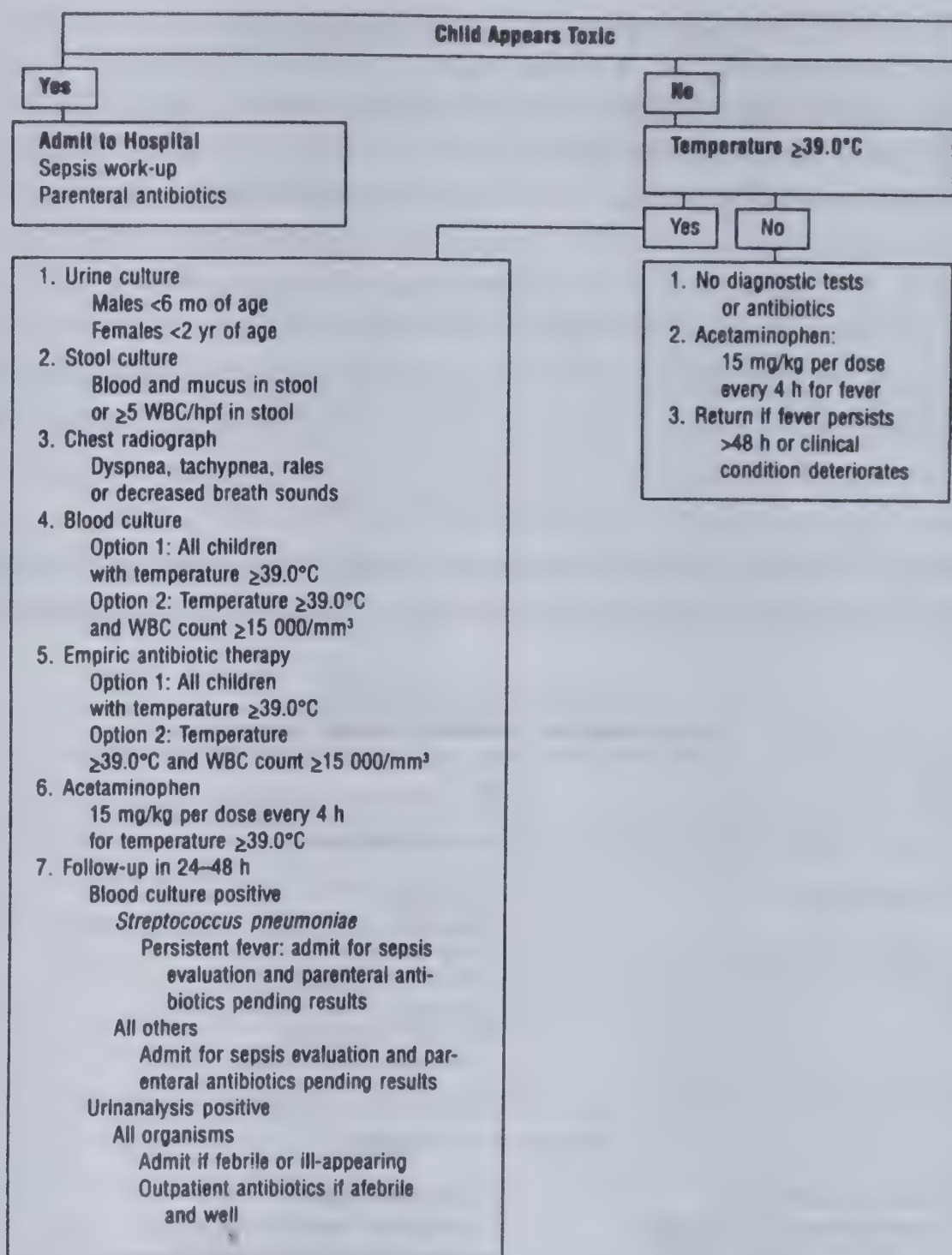


Figure 41.2. Algorithm for the management of a previously healthy child 91 days to 36 months of age with fever without source. (Reprinted with permission from the American Board of Family Practice. March-April 1995;8(2):117.)

respiratory rate $>60/\text{minute}$, grunting, cyanosis, nasal flaring, and/or intercostal retractions. History includes specific questions asked about prematurity, maternal fever, premature rupture of membranes (PROM), presence of meconium at delivery, and family history of congenital heart disease. Noncardiopulmonary causes will usually be apparent by history or simple laboratory testing, such as distress in an infant born to a mother with PROM or diagnosis of hypoglycemia by capillary sample.

Upper respiratory tract causes of respiratory distress include choanal atresia, the most common congenital anomaly of the nose. The classic presentation is an infant in distress with cyanosis that clears with crying. Diagnosis is made by the inability to pass a catheter through the nostrils.

Lower respiratory tract conditions in the term infant include Respiratory Distress Syndrome (RDS), transient tachypnea of the newborn (TTN), pneumonia, fluid aspiration, and pneumothorax. Standard diagnostic tests include chest x-ray (CXR), arterial blood gases, CBC with differential, glucose, blood cultures, and other work as clinically indicated.

Respiratory Distress Syndrome (RDS). RDS, also known as hyaline membrane disease, is a major cause of morbidity and mortality in premature infants but can occur in term infants also. The underlying problem is pulmonary immaturity and surfactant deficiency. Infants work hard to breathe due to the reduced lung compliance and can tire quickly, leading to total respiratory collapse. Diagnosis is usually made by history and a classic diffuse bilateral atelectasis causing a “ground glass” appearance on chest x-ray. Treatment depends on adequate supplemental oxygen, nutritional support if needed, intubation for respiratory failure, and artificial surfactant.

Transient Tachypnea of the Newborn (TTN). TTN usually consists of mild to moderate respiratory distress in infants born by cesarean section but can occur in an uneventful term delivery. The distress usually occurs in the first few hours of life. The exact etiology is unclear but may be due to incomplete resorption of fetal lung fluid. All symptoms of respiratory distress can be present, and it may be difficult if not impossible to distinguish from more severe conditions. Keys to the diagnosis include the rapid improvement in 1 to 2 days and prominent perihilar streaking and fluid in the interlobar fissures on chest x-ray. Treatment depends on respiratory support during the initial presentation, but the infant may need a full diagnostic evaluation including cultures, laboratory work, until the diagnosis is clearer.

Pneumonia. The lungs are the most common site of infection in the neonate. Risk factors for the development of pneumonia in the infant include membranes ruptured longer than 12 to 18 hours before delivery, premature rupture of membranes, and active infection in the mother. Common pathogens include Group

B Streptococcus, E.coli, Chlamydia, and staphylococcus aureus. CXR may show an active disease process, but there are no signs pathognomonic of pneumonia. Diagnosis is made by history and physical, blood cultures, CXR, ABGs, CBC with differential, with Gram's staining of tracheal or gastric aspirate sometimes helpful. Empiric treatment with antibiotics is essential.

Meconium Aspiration. Meconium is present in amniotic fluid in approximately 10% of all deliveries. Five in 1000 infants with meconium-stained fluid will have meconium in the trachea. The course of these infants is often characterized by decreased APGAR scores at birth and immediate respiratory distress. Chest x-rays often show irregular distribution of infiltrates and areas of overexpansion. Treatment involves amnioinfusion during labor for thick meconium or with moderate meconium and variable decelerations of the fetal heart tones. The infant should undergo DeLee suctioning on the perineum with visualization of the cords and tracheal suctioning before stimulation. Oxygen support and antibiotics may be needed although infants usually improve within 48 hours unless infection is present.

Pneumothorax. Lung collapse of some degree may be seen in 1% of all deliveries and is usually not significant. If severe enough however, profound distress may follow. Breath sounds will be asymmetric, and the mediastinum may be shifted. CXRs will be diagnostic. Therapy depends on the severity of the collapse, ranging from oxygen support and observation to the placement of chest tubes.

Hyperbilirubinemia. Hyperbilirubinemia is the most common diagnosis in the newborn period, and any level of bilirubin high enough to discolor the skin or sclera produces the characteristic jaundiced appearance. Hyperbilirubinemia can be divided into three categories for the purpose of diagnoses and evaluation: physiologic, nonphysiologic (pathologic), or breast-milk.

Physiologic Jaundice

Physiologic jaundice may occur in 50% to 60% of normal infants. Underlying conditions that predispose otherwise well infants to jaundice include increased bilirubin loads due to reduced fetal red blood cell survival, immature liver function resulting in reduced clearance, and slower gut motility, which results in in-

creased resorption of bilirubin. Characteristically, the jaundice appears after the first day of life, peaks between days 3 to 5, and disappears by day 10. Bilirubin levels rarely exceed 12 to 13 mg/dL and consists almost entirely of unconjugated fraction. No further work-up is required with this clinical presentation.

Nonphysiologic Jaundice (Pathologic). Pathologic jaundice occurs on the first day of life, and bilirubin fractions will be significant for direct bilirubin exceeding 1.5 to 2.0 mg/dL. The underlying problem is an overabundance of bilirubin. Etiologies include, but are not limited to, sepsis, polycythemia, ABO incompatibility, hemolysis, and spherocytosis. Other conditions result in abnormal bilirubin metabolism such as hypothyroidism, galactosemia, and deficiency in glucose-6-phosphate dehydrogenase, which increases bilirubin levels. Total serum bilirubin levels may rise by more than 5 mg/dL/day, exceed 12 mg/dL, and persist longer than 10 days in term babies and 14 in premature infants.

Laboratory evaluation includes a CBC with differential, reticulocyte count, total and direct bilirubin, blood type and Rh of both infant and mother, and Coombs' test. Other tests depend on history and clinical signs, such as blood cultures for suspected cases of sepsis. The primary goal of treatment is to prevent kernicterus, the deposition of unconjugated bilirubin into the central nervous system. Unfortunately, treatment levels must be individualized as there is no specific danger level for every infant.

Phototherapy remains the mainstay to treatment. Phototherapy converts unconjugated bilirubin in the skin to a water-soluble form, which can be excreted in the stool and urine. The physician must provide adequate nutrition and increased fluid support during treatment and check bilirubin levels every 4 to 6 hours. Care must also be taken to shield the eyes and genitalia of the infant while under the bilirubin lights. Exchange transfusions are reserved for those infants who have failed phototherapy or have severe hemolytic disease. This is a procedure that should be done in an intensive care setting by someone experienced with the technique.

Breast-milk jaundice. Breast-milk jaundice can be distinguished from other types by the late appearance, usually between 6 to 14 days, in an otherwise healthy, breast-feeding baby. The jaundice is secondary to increased unconjugated bilirubin fractions and can be accentuated by physiologic jaundice. Bilirubin levels are usually

in the range of 10 to 15 mg/dL. Kernicterus has never been reported from this condition, and phototherapy is not indicated. Treatment consists of substituting formula for breast milk for 2 to 3 days, as cow's milk formulas inhibit the absorption of unconjugated bilirubin from the intestine. Serum bilirubin levels rarely rise to significant levels when breast feeding is resumed.

Pyloric Stenosis

Pyloric stenosis is a condition of unknown etiology that is more common in first-born infants and in males. The usual history is of an infant who had been previously well that develops progressively severe vomiting. Constipation, weight loss, and dehydration follow. Upon examination the child appears ill, and a classic finding is a palpable olive-sized mass in the right upper quadrant that represents the hypertrophic pylorus. This will be present in more than 95% of patients. Abdominal ultrasound may be helpful but will miss 8% of children with pyloric stenosis. Gastrointestinal imaging should be done only if the pyloric mass cannot be palpated or if the diagnosis is unclear. Treatment consists of correcting fluid deficits and electrolyte problems, and pyloromyotomy. Long-term prognosis after surgery is excellent.

Intussusception

Intussusception is the most common cause of intestinal obstruction in children under 2 years of age, and has a peak incidence in infants 5 to 9 months old. Adjacent bowel segments telescope onto one another, and in 95% of cases no underlying cause is found. Parents relate a history of an infant who suddenly develops vomiting and abdominal pain, followed by bloody bowel movements. On examination the abdomen is tender and a mass may be felt, usually in the upper mid-abdomen. Reduction of the intussusception can be done by barium enema, which may also be diagnostic. Surgery is required if the enema reduction fails or perforation exists.

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Preventive Care of the Preschool Child (1–5 Years)

Kurt Kurowski

COMMON HEALTH AND PREVENTION ISSUES IN THE 1–5-YEAR AGE GROUP

Accidents and Injuries and Their Prevention

Injury is the leading cause of mortality for children in the United States, accounting for 30% of all deaths in this age group and many more emergency room visits and hospitalizations for the nonfatal injuries (1, 2). Injury and death rates from injuries are higher for black and nonblack minority children, as well as for children who live on farms. The largest number of injury deaths are seen in children who are in motor vehicle accidents (either as an occupant of the vehicle or a pedestrian), followed by burns, drowning, victims of violence, or falls.

Motor Vehicle Accidents

Motor vehicle accidents account for the largest proportion of injury deaths to children (47%) (3). Fatalities are decreased by the use of child safety seats (4). Children should always be secured in child safety seats when in a motor vehicle, as required by law in all 50 states and the District of Columbia. Children over the age of 4 are best protected by a combination of safety belt use and automobile air bags. Alcohol is a major contributor to automobile injuries, especially those involving fatalities. Most such pediatric deaths occur when the child is a passenger in a car with a driver who has been drinking (5).

Drowning and Near Drowning

Children ages 1 to 3 have the highest drowning death rate. About 90% of childhood drownings occur in residential swimming pools. Only about 4% of these drownings occurred in above-ground pools (6). There are approximately 4 near-drowning cases for every drowning mortality. Whereas most near-drowning victims recover completely, about 20% of those children requiring hospitalization after near-drowning episodes have severe permanent brain damage. Recovery without neurologic sequelae is unusual after immersions of greater than 5 minutes or if the patient does not show a return of spontaneous respirations within 2 minutes of starting cardiopulmonary resuscitation (CPR). A fence surrounding the pool with a self-latching gate reduces by about 50% the rates for near drownings and drownings in households with residential pools (7). Pool fences should probably be at least 4.5 feet in height and ideally should be within a separate yard fence with its own self-latching gate. Widespread training in CPR, especially among pool owners, may also improve outcomes (8).

Burns

Most childhood deaths from burns occur in children less than 4 years of age. The annual death rate from burns and fire for children in this age group is about 4.7 per 100,000. Childhood deaths secondary to a burn or fire are more common in black children (9). For every burn-related childhood death there are many more hospitalizations and still more outpatient treatments. Most children less than age 4 who are hospitalized for burns receive their burns from hot liquids.

Preventive strategies include decreasing hot water heater temperature to less than 120°F. Antiscald devices can be placed on showers and faucets. Smoke detectors should be installed on each floor, and battery status should be frequently checked. Cigarette lighters can be designed with "childproof" features and even the cigarettes themselves can be manufactured to decrease the chances of them igniting sofas and mattresses (10).

Growth

One of the key parameters being tracked during well-child visits are growth parameters such as length, weight, and head circumference.

Height (or length) is best assessed by taking measurements

at birth and at each well-child visit and plotting these values on standardized growth curves. For an infant born prematurely, adjustment for its gestational age must be done by subtracting the number of weeks it was born prematurely from their postnatal age and using this corrected age on the age axis of the standardized growth curve to find its percentile for height. If the child is less than 5% or greater than 95% for height, a correction for the parental height of his or her parents should be made. This is done by calculating the midparental height, which is the sum of the two parents' heights divided by two, and then using the combination curve of Tanner (Fig. 42.1) to find the percentile of the child's height in relation to the midparental height. A correction of the height for the sex of the child must be made by subtracting 13 cm from the father's height for a female child and adding 13 cm to the mother's height for a male child (Table 42.1).

Head circumference (occipitofrontal) should be measured with a tape measure at each well-child visit up to age 2 and plotted on standardized curves. Macrocephaly and microcephaly are defined as head circumferences 2 standard deviations greater or less than the 50th percentile for the child's age, respectively (Table 42.2).

LEAD POISONING

About 17% of children in the United States are at risk for lead toxicity (11). The developing nervous system of young children is particularly sensitive to lead. Prolonged levels greater than 10 to 15 micrograms per deciliter are associated with behavioral and cognitive defects. Peak levels of lead are seen in children ages 1½ to 2 years. Lead can be absorbed through the respiratory tract as well as the GI tract; but with the elimination of lead in gasoline, the most common sources for lead in children are old paint (pre-1960), soil, house dust, lead-based solder for pipes, and battery casing. The major route of transmission in children is hand to mouth.

Most children with lesser degrees of lead elevation are asymptomatic. Early effects are delays in developmental milestones (e.g., speech) or the loss of previously attained developmental milestones. Children with higher levels (greater than 30 to 40 micrograms per deciliter) may experience anorexia, irritability, sleep disturbances, vomiting, constipation, and abdominal pain. Children with acute lead encephalopathy (usually seen

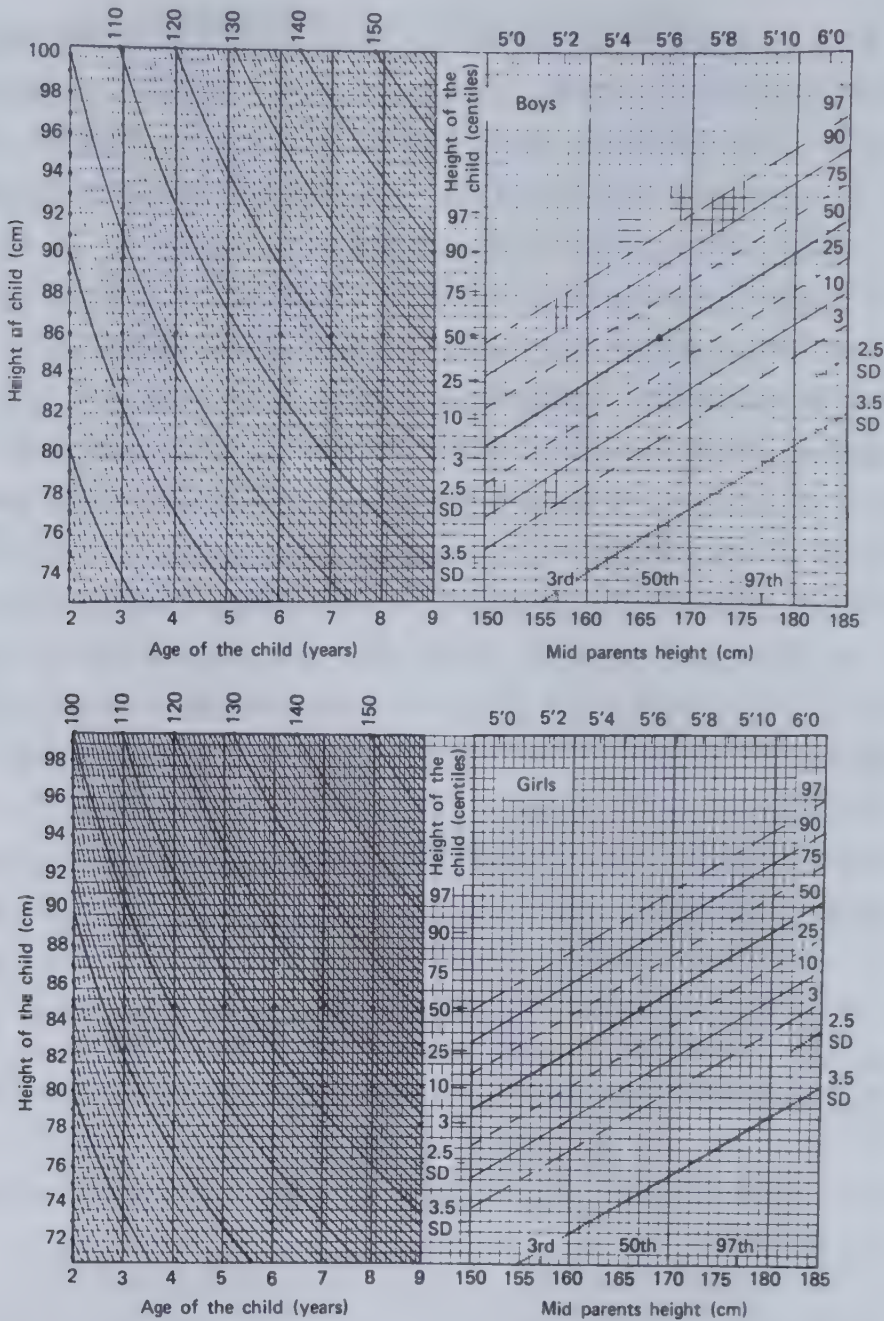


Figure 42.1. Tanner's diagram for evaluation of a child's height in relation to parent's height. From the child's height (ordinate, left panel), the curve crosses the child's age (abscissa, left panel) at a given point. This point is reported on the right panel, on the vertical line corresponding to the mid parents' height, thus giving the percentile or standard deviation of the child's height as a function of the parents' height (ordinate, right panel). Reprinted with permission from Tanner et al. *Preventive care of the preschool child*. Oxford: Blackwell Scientific Publications, 1970.

only if lead levels are greater than $100 \mu\text{g}/\text{dL}$) will display emesis, lethargy, and seizures.

Physical examination in children with lead poisoning usually shows no specific changes if elevations are mild. With high blood levels, ataxia, lethargy, and delirium can be observed as well as Burton's lines (blue-black lines on the gums visible at the tooth insertion margins). Recent evidence suggests that behavioral problems in boys 7 to 11 years old may be associated with chronic lead intoxication as measured in bone deposits (12).

Table 42.1.**Differential diagnoses for short child.****Low rate of growth and absence of morphologic aberrations**

1. Malnutrition (usually purely caloric although Fe and Zn deficiencies are being increasingly recognized)
2. Chronic systemic diseases (e.g., cyanotic heart disease, renal failure, HIV infection)
3. Parental deprivation (e.g., parent is drug abuser, poor economic and social support for child)
4. Endocrine etiology (growth hormone deficiency, Cushing's disease, pseudohypoparathyroidism)
5. Turner's syndrome (other features of the syndrome may be absent)

Normal rate of growth and absence of morphologic aberrations

1. Intrauterine growth retardation (small for gestational age or <2000g at birth)
2. Genetic short stature
3. Delay in adolescent growth spurt and puberty (rate of growth is normal for bone age; usually child's parents have history of similar delay)

Morphologic aberrations present or disproportionate appearance

1. Skeletal dysplasias (e.g., achondroplastic dwarf)
2. Chromosomal abnormalities (Down's syndrome, Turner's syndrome)
3. Syndromes associated with short stature (Prader-Willi, Bloom)

Differential diagnosis for tall child.**Increased rate of growth and absence of morphologic aberrations**

1. Precocious puberty (bone age is greater than chronological age here, final adult height will be low because of premature closure of epiphyses)
2. Increased growth hormone (usually secondary to pituitary adenoma)
3. Hyperthyroidism

Normal rate of growth and absence of morphologic aberrations

1. Genetic tall stature (most common etiology for tall child)

Disproportionate appearance or morphologic aberrations

1. Marfan syndrome (long arm spans, arachnodactyly, ectopic lens, autosomal dominant but many cases represent spontaneous mutations)
2. Klinefelter syndrome (particularly increases long bone length in legs)
3. Sotos syndrome (large forehead and ears, mental retardation)

The only significant laboratory abnormality in children with mild elevations of lead will be a whole blood lead level of 10 to 20 $\mu\text{g}/\text{dL}$. With higher blood levels of lead, a mild hypochromic anemia with basophilic stippling, disturbed lines of osteogenesis in the metaphyses of the long bones on x-ray, and visible ingested

Table 42.2.**Differential diagnoses for macrocephaly.**

Familial (the parent's head sizes should be measured and plotted if this is suspected)

Primary megalencephaly (a diffuse increase in all intracranial neural elements, often autosomal dominant transmission, some cases associated with seizures, mental retardation, and cortical spinal dysfunction)

Hydrocephalus (child may be more irritable or lethargic and may have projectile vomiting; if less than 6 months of age, a bulging anterior fontanelle will be the first physical sign). Cranial ultrasound can be used to evaluate for hydrocephalus if the cranial sutures are still open)

Noncommunicating hydrocephalus (a block in flow within the ventricular system) (most commonly at aqueduct)

Communicating hydrocephalus (a block in absorption at the arachnoid granulations secondary to previous meningitis or subarachnoid hemorrhage or infiltration by leukemia or lymphoma)

Increased CSF production (from choroid plexus papillomas)

Infectious

Congenital infection with toxoplasmosis, rubella, CMV virus, herpes virus or syphilis more likely to produce microcephaly but may lead to secondary macrocephaly. TORCHS' titers should be checked

Neoplastic

Postintracerebral hemorrhage (as seen in neonates, especially those born premature)

Metabolic/storage diseases

Tuberous sclerosis (children may also have seizures, mental retardation and adenoma sebaceum)

Neurofibromatosis

Differential diagnoses for microcephaly.

Familial (parents will have similar smaller head size)

Microcephaly may be only abnormality with normal intelligence

Microcephaly can be seen along with seizure disorders and mental retardation in other families

Intrauterine drug and radiation exposures

Alcohol, tobacco, cocaine

Intrauterine infections

TORCHS' agents

HIV

Perinatal asphyxia

e.g., placental infarction or abruption

Chromosomal abnormality

e.g., Trisomy 18, Trisomy 13

Neuronal migration disorder

e.g., polymicrogyria

Syndromes associated with microcephaly

e.g., Cornelia de Lange, Prader-Willi

Maternal metabolic derangements

e.g., maternal phenylketonuria, diabetes mellitus, or uremia

lead within the intestine and visible on plain abdominal radiographs can sometimes be seen.

Treatment

Sources of lead in the child's environment must be removed with the help of public-health agency personnel. The dwelling is completely vacuumed with a high-efficiency particle accumulator vacuum, then washed with a phosphate detergent, and revacuumed. These areas are then repainted using encapsulant paint. Intravenous chelation therapy with calcium EDTA or DMSA (2,3-dimercaptosuccinic acid) or the oral chelator Succimer is reserved for children with symptoms or lead levels greater than $45 \mu\text{g/dL}$. Children with moderate elevations (20 to $25 \mu\text{g/dL}$) are managed with environmental changes and sometimes the oral chelator D-penicillamine and close follow-up (weekly initially) to ensure a drop in blood lead levels to at least $15 \mu\text{g/dL}$.

Screening

Blood lead levels should be obtained in all children demonstrating possible symptoms of lead exposure or demonstrating a lot of hand-to-mouth activity. Levels are checked at ages 1 and 2. More frequent monitoring should start at age 6 months if child lives in or regularly visits a dwelling built before 1960 with peeling paint or being actively remodeled or repainted, or where another child or adult in the household has known increased lead exposure, or lives near an industrial source of lead (e.g., smelting plant, battery recycling) (13).

IRON DEFICIENCY

A deficiency in iron is the most common nutritional deficiency in childhood. It reaches its highest prevalence of 30% at age 1 to $1\frac{1}{2}$ years. Iron is a crucial component of the hemoglobin molecule but is also a necessary component of myoglobin and several enzymatic systems including the cytochromes. If absorption of iron is inadequate for needs and losses the following course of events will transpire in sequence:

- Decrease in Fe stores in liver and bone marrow with decreased serum ferritin level.

- Decreased serum Fe level with an increase in total iron-binding capacity and a decrease in transferrin distribution.

Development of microcytosis with a decrease in MCHC (mean corpuscular hemoglobin concentration), and because of the vast variety of sizes of RBCs in the circulation, an increase in the measured RDW (red cell width distribution).

Decreased hemoglobin and hematocrit with thrombocytosis.

Unfortunately, there are adverse effects on attention, behavior, and school performance for children with iron deficiency even if the child is not anemic (14, 15).

Absorption of iron is highly variable, depending on the chemical form of the ingested iron, present body stores, and other ingested nutrients (e.g., dietary ascorbic acid will increase Fe absorption). Because of lactoferrin present in breast milk, which binds to specific intestinal receptors, the low levels of iron present are particularly well-absorbed (16). This is not the case for cow's milk. The heme iron in animal tissues is also well-absorbed.

An infant's iron stores are usually adequate for the first 6 months of life unless the child was born premature or has lost iron through blood loss. Iron deficiency is more common in a premature infant, as this shortens the period of iron extraction from the mother. Blood loss during infancy is commonly caused by a reaction to a protein in cow's milk producing a mild but chronic GI blood loss. These two groups require iron supplementation during the first 6 months. This can be done by encouraging breast feeding, using an iron-fortified formula (10 to 12 mg of Fe per liter of formula), or giving the child daily multivitamin drops with iron. The prevalence of iron deficiency increases after 6 months of age, with the likelihood increasing if the child was not breast-fed during the first 4 months, or if there was an introduction of cow's milk at ≤ 9 months of age). Iron-rich food introduced at 6 months will decrease this risk.

Children with early stages of iron deficiency will be asymptomatic, making attention to risk factors and screening important. Profoundly depleted children might exhibit irritability, anorexia, and pica. Superimposed lead toxicity is frequent in these children. They may demonstrate pallor, tachycardia, systolic "flow" murmurs, and/or splenomegaly. A CBC is recommended in all children at age 1 with checks also at 6 months and 2 years for higher risk children (premature infants, known episodes of blood loss).

IMMUNIZATIONS

Varicella Vaccine

This is a live attenuated viral vaccine that in healthy children produces initial seroconversion in $>95\%$ and clinical protection rates $>85\%$ (15). Routine immunization has been recommended for children between ages 12 and 15 months, but long-term clinical follow-up studies on these children have not yet been done. The timing and efficacy of booster immunizations has not been studied either. Naturally acquired varicella produces life-long immunity, and the disease is well-tolerated by almost all healthy children; some question the wisdom of temporarily “protecting” children, as their immunity might fade in adulthood when the incidence of complications with varicella greatly increases. Complications of varicella include encephalitis, aseptic meningitis, Reye’s syndrome, pneumonia, thrombocytopenia. There is also a congenital varicella syndrome (cicatricial scars, limb hypoplasia, seizures, mental retardation). The vaccine might be more logically used only for adults who have never had varicella; two doses are given, 1 to 2 months apart. The vaccine is not licensed for immunocompromised patients in the United States. The vaccine is contraindicated during pregnancy, and aspirin should be avoided for 6 weeks postimmunization due to concerns producing Reye’s syndrome.

Measles, Mumps, Rubella Vaccination (MMR)

This is a combination live attenuated viral vaccine. The first dose is given at age 15 months. (The proportion of children who seroconvert in response to the measles component decreases progressively if the child is younger than this.) However, if there is a high incidence of preschool measles within the community, a separate initial measles vaccine can be given at 12 months, and in the face of a measles epidemic, a separate measles vaccine can be given at 6 months. These children still receive the MMR at 15 months. Immunity is known to wane after about 10 years. A booster vaccine is therefore recommended by some at age 12 to increase protection during high school and college, whereas others advocate giving the booster at the earlier age 4 to 6 because of believed better compliance, giving this booster along with the child’s other preschool immunizations. Side effects of the MMR vaccination include fever, a 10% incidence of a measles like rash, rare occurrences of encephalitis (1:1,000,000), arthalgias and arthritis, and peripheral

neuropathies. Contraindications include known anaphylactic reactions to eggs or neomycin, pregnancy (theoretically), severe febrile illness, and immune deficiency (although it may be given to patients who are in the asymptomatic stages of HIV infection).

Well-Child Visit Checklist

Age	Developmental Skills	Lab / Immunization Issues	Special Concerns
1 year	Stands alone for a few seconds Speaks 2–3 words with meaning Will bang 2 blocks together	PPD skin test Hgb or Hct Blood lead level Sick cell screen (if high-risk)	Conversion from formula to milk Check muscle tone Check for intoeing Child taking all food classes (but no hot dogs, nuts or popcorn) Lock up of all potential toxins; use car seat
15 months	Walks and runs Speaks 4–6 words Forms 2-block tower Removes own clothes Uses eating utensils	MMR (1) Hib conjugate vaccine (2)	Syrup of ipecac in house
18 months	Walks up steps Forms 4-block tower	DPaT (or DPT) (3) OPV or IPV (4)	
2 years	Combines words Names body parts Throws ball overhand Puts on clothes (with help)		Toilet training started Tantrums common Engineered safety to keep from street, pool
2½ years	Understandable speech Jumps		1st efforts at vision screening 1st dental evaluation Note: only 75% of boys and 90% of girls have bowel control here

Age	Developmental Skills	Lab / Immunization Issues	Special Concerns
3 years	Forms 3–4-word sentences Pedals cycle 1/3 of children have poor nighttime bladder control		Consistency in discipline important between parents Child starting to understand right and wrong
4 years	Walks up and down stairs Stands on one foot for a few seconds Counts 1–5 Holds basic conversations	DPaT (or DPT) OPV(or IPV) (4) increases Cholesterol screen (if positive family Hx)	Dental caries risk
5 years	Understands opposites Can draw person	MMR booster	Understands right vs. wrong

1. MMR is combined measles, mumps, rubella live attenuated viral vaccine.

2. Hib conjugate vaccine is a Haemophilus influenza type b capsular antigen that is conjugated to T-cell-dependent protein antigens to improve immunogenicity in children less than 18 months (where most of the invasive *H. influenzae* disease occurs).

3. DPaT is a combination diphtheria toxoid, acellular pertussis antigen, and tetanus toxoid vaccine. Initial trials have shown it to be less clinically effective in preventing whooping cough than the whole cell Pertussis vaccines in children less than age 1, and the traditional primary series with DPT (the whole cell Pertussis vaccine) is still recommended for vaccination at ages 2, 4, and 6 months. For booster vaccinations after 1 year of age, DPaT is preferred, as it gives equal protection and significantly less local (erythema and tenderness at injection site) and systemic (fever, drowsiness) side effects (17). Children less than age 7 not immunized against DPT during their 1st year and who have no contraindications to the vaccine should be given a DPT vaccine (the acellular Pertussis can be substituted once the child has reached age 15 months) when seen with follow-up vaccine 2 months, 4 months and 16 months after the 1st DPT in the series was given with a booster dose at age 4–6 years.

Anaphylactic reactions or encephalopathy or altered consciousness or seizures lasting greater than 24 hours after receiving DPT or DPaT remain contraindications to further doses.

4. OPV is oral polio vaccine (a live attenuated viral vaccine containing attenuated strains of polioviruses 1, 2, and 3). Fecal viral shedding occurs for weeks after this vaccine. IPV is inactivated poliovirus vaccine. It is a parenteral vaccine that has greater potency than the older preparations. The dose schedule for both vaccines is the same. Although very rare (incidence about one case in 2.5 million vaccinations), oral polio vaccine-associated polio is essentially the only source of new polio cases in the United States. Vaccine-associated polio has not been reported with IPV. Presently IPV instead of OPV is recommended for children with or living in a household with an immune deficient person, in-

cluding HIV, or adults who were never immunized for polio and are now at risk for exposure. Since 80% to 90% of oral polio-associated polio occur after the first dose, it is suspected that vaccination recommendations will change for other children to a schedule of IPV for the first doses at ages 2 and 4 months of age, with OPV for all subsequent doses. Children less than age 7 not immunized against polio during their 1st year and who have no contraindications to the vaccine should receive OPV (or IPV) at the 1st visit and 2 months and 16 months after the 1st dose was given. If the child is not age 4 or older when the 16-month dose is given, a booster (OPV or IPV) should be given at 4–6 years of age.

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Preventive Care of the Child Through the Latent Years (5–12)

Mary Jo Welker

While the ages 5 to 12 have been identified as the latent years, there is actually much to be monitored, and many changes take place during these years. These include tremendous growth, the beginning of sexual change, and the stress of starting and adapting to school and socialization. As children become exposed to risky behavior patterns at an earlier age, the counseling for the parents and children becomes more important. As prevention and screening are addressed, unless otherwise specified, the recommendations are based on the 1996 U.S. Preventive Services Task Force (1).

ACCIDENT PREVENTION

Motor Vehicle Accidents

Motor vehicle accidents are the leading cause of death in children (2). With this thought in mind, it is essential to counsel children who have outgrown safety seats, and their parents, on the use of lap/shoulder/safety belts. It is also important to remind them not to ride in the cargo beds of pickup trucks, nor of station wagons or vans unless they are fitted with passenger seats and proper restraints.

Discussion of motor vehicle safety also presents an opportunity to remind parents not to drive while under the influence of

alcohol or other drugs and to remind motorcycle drivers of the importance of helmets, for both them and their children. Since many injuries are to pedestrians, it is important to remind parents of the limited skills of young children, and the supervision necessary to protect children from pedestrian injuries.

Fires and Burns

Burns from fire are the second most common cause of unintentional injury in children, and are most commonly residential in occurrence (3). Matches and lighters should be stored safely out of the reach of children (see Chapter 42).

Drowning

Pools should have isolation fences with locks, and children should be supervised when they are swimming. Children should be taught to swim, and taught water safety at an early age to minimize injuries. Safe boating practices should be observed when on the water, and flotation devices should be worn to prevent drowning.

Firearms

Guns should be stored unloaded, and locked in a compartment where children will not have access to them.

Poisoning

All medications and toxic substances should be stored in child-resistant containers and out of reach of children, ideally locked in a cabinet. Syrup of ipecac should be kept in the home, and the number for the local poison control center should be immediately available. Stickers to indicate toxic substances have not proved to be effective in prevention of poisoning (4).

Bicycle Injuries

Fifty percent to eighty-five percent of bicycle fatalities are related to head injuries (5), and bicycle helmets can reduce head injuries by 40% (6). It becomes essential to counsel children and their parents on the importance of wearing bicycle helmets for injury prevention. Bicycle safety training can also be helpful in preventing injuries. Finally, avoiding areas of motor vehicle traf-

fic can be effective, since 95% of fatalities are the result of the collision of a bicycle with a motor vehicle (6).

SCREENING EXAMINATIONS

History should be updated yearly, and includes the family history, a review of systems, and questions about school, exercise, diet, and other concerns. The history helps determine which screening tests may be necessary as part of the prevention plan.

Blood Pressure

Children should have blood pressure recording performed every 1 to 2 years during regular office visits. It is important to remember that children have great variations in blood pressure based on age, sex, height, and weight (7). However, unlike in adults in whom 95% of hypertension is idiopathic, in children secondary causes of hypertension account for 28% of this diagnosis (8). For example, coarctation of the aorta can be identified in children, and delayed repair increases the risk of irreversible hypertension. The diagnosis of hypertension is still made with recording on three separate visits 1 month apart. Table 9.3 gives normal and hypertensive pressures of various age ranges.

Growth and Development

During these years children maintain a steady growth that averages roughly 2 1/2 inches/year from age 5, subsiding gradually in both sexes to 2 inches/year by age 10. The rate remains flat through age 12 for boys, while girls spurt back to 2 1/2 inches between 11 and 12 as they enter adolescence. During the same period boys' and girls' weights on average accelerate from 5 lb. gain per year at 5 years of age at the rate of 1/2 lb./year per year so that at the age of 10 they are gaining 7 lbs.; boys maintain the same rate of acceleration, gaining 9 lbs./year at age 12, while girls spurt to 11 lbs. per year at ages 11 and 12 (9). All children should have height and weight measured annually and plotted on a growth chart indicating age, height, and gender in order to assist in determining appropriate growth as well as screen for obesity. It is estimated that 5% to 25% of children are overweight, and the percentage is thought to be increasing (10-11). Evaluations for insufficient or excessive growth are outlined in Chapter 34.

A great deal of development occurs during the school years. Motor skills become more specialized as children experience more structured activities. Cognitive and social development varies greatly among children, and is most often assessed in the school setting. Numerous developmental dysfunctions have been identified in school-aged children, and are beyond the scope of this chapter. However, when behavior problems, attention deficit disorders (ADD), or other school performance problems are brought to the attention of the physician, they should be evaluated appropriately. Intervention in the form of school adaptations, counseling for the child and family, and the possibility of medication may all be considered.

Though ADD has its onset virtually as early as personality formation, in practical terms it begins in this age group with school attendance. ADD prevalence may be as high as 5%, with males:females $\geq 6:1$. The disorder may not be apparent in one-on-one situations that are novel to the child (e.g., the doctor's office). Most often the teacher alerts the parents to the problem because of observation of varying degrees of the cardinal manifestations of ADD: hyperactivity, distractibility, short attention span, restlessness, impulsiveness, antisocial acting out, learning disability, and poor academic performance. For refinement in diagnosis the practitioner is referred to pediatric neurology or to the Conners' Teacher Rating Scale (C. Keith Conners, Ph.D., Department of Psychiatry, Duke University Medical Center, Durham, NC 27710).

Scoliosis

Congenital scoliosis has its onset between the ages of 8 and 10, males:females = 4:1 prevalence. There are various recommendations for screening for this condition. The American Academy of Pediatrics recommends screening all children with forward bending at ages 10, 12, 14, and 16 years of age. A positive test, with the child bending forward 90%, hands clasped, consists of asymmetry in the heights of the ribs. Bracing is indicated for primary curvature in the 20% to 40% range (frontal plane, thoracic spine x-ray) and surgical correction for $>40\%$; for $<20\%$, x-rays should be repeated yearly until adolescence, at which time they should be done every 4 to 6 months. A more conservative view is held by the U.S. Preventive Services Task Force, which states "there is insufficient evidence to recommend for or against routine screening of asymptomatic adolescents for idiopathic scol-

iosis" (1), visually inspecting the back for scoliosis when other examinations are being performed. Many school nurses are currently performing this screening, and children are referred to the physician for evaluation of this problem.

Sexual Development

Sexual development occurs in older children, about the ages of 10 to 12 years. Screening for sexual maturity is based on secondary sexual characteristics. Changes in breast configuration and pubic hair are used to evaluate maturity in females, as are changes in genital organs (penis and testes) and pubic hair in males. Sexual maturity ratings range from 1 to 5, with 1 indicating the prepubertal state and 5 being adult development. (See Chapter 34 for Tanner maturation scale.)

Children should be informed about the changes in their bodies that will occur during this time, and concerns should be addressed openly and honestly. Appropriate sexual counseling may be necessary in certain older children. Information about prevention of pregnancy and safe sex for the prevention of sexually transmitted diseases should be offered to sexually active individuals.

Dental

It is during this age span that secondary teeth replace primary teeth, and they emerge in about the same order as the primary teeth emerged (see Chapter 2).

Tuberculosis

There is no recommendation for routine screening of this age group for tuberculosis. However, screening by skin test should be done for high-risk populations. This includes patients with HIV disease, contacts of patients with tuberculosis, immigrants from countries with a high incidence of tuberculosis, medically underserved and low-income individuals, individuals with medical risk factors associated with tuberculosis, and residents of high-risk facilities. All positive tests should be evaluated and treated appropriately.

Cholesterol

The recent U.S. Preventive Services Task Force states that there is insufficient evidence to recommend for or against routine

cholesterol screening in children and adolescents (1). Others recommend selective screening of children if there is a family history of premature coronary artery disease or of hypercholesterolemia. The benefits of screening in children are uncertain, and the risks of drug therapy and the limited success of dietary counseling in this age group suggest that widespread screening may lead to more harm than good.

Urinalysis

There are no recommendations for routine testing of the urine in children in this age group, either for infection or other diseases.

Hearing

Routine screening for hearing abnormalities in asymptomatic individuals in this age group is not recommended by the U.S. Preventive Services Task Force. However, the American Academy of Pediatrics recommends routine historical questioning regarding hearing problems and testing at age 5, 10, and 12. Clinicians also should be alert for any signs or symptoms of hearing loss. Screening tests are done at many schools, and abnormals should be followed.

Vision

There is no recommendation for or against routine screening of asymptomatic children in this age group. Clinicians should inquire about symptoms in taking the history, and symptomatic children should be tested. As of 1992, schools in all but 12 states did routine screening of school-aged children, and abnormals should be followed up appropriately.

Violence - Child Abuse

The U.S. Preventive Services Task Force again states that there is insufficient evidence to recommend for or against screening questionnaires for child abuse in this population. The data suggest there are few reliable techniques, and it is difficult to get evidence. Clinicians should be alert to the presentations of childhood abuse, both physical and sexual. During history taking it is appropriate to ask questions about discipline of the children, and about history of abuse in the parents. It is important to remem-

ber that some victims of abuse have no physical findings, especially in sexual abuse. Be aware of burns, bruises, and lesions that have particular appearances (e.g., cigarette burns, bruises shaped like hands). Also be aware of multiple or repeated injuries.

Sexually Transmitted Diseases

Testing for gonorrhea, chlamydia, and herpes should be available and offered to older children who are sexually active or to high-risk groups, or children who have been the victims of sexual abuse.

Skin Cancer

It is important to remind children and their parents of the dangers of ultraviolet light. They should be reminded to wear sunscreens and light clothing to prevent sunburns, which may increase the risk of later skin cancers.

Smoking

Approximately 25% of children ages 12 to 13 have experimented with smoking, and 4% are regular smokers (12). It is therefore important to deliver antitobacco messages to children and adolescents. It is also important to help them develop skills to resist the social pressure to use tobacco and to remind them of the short-term and the long-term consequences of tobacco use. These messages need to be repeated over time in order to prevent the institution of tobacco use in older children. School-based programs are also available to help prevent or delay initiation of tobacco use, and clinicians should be aware of these programs and supportive of them. Children also present an opportunity to remind parents who smoke about the adverse effects of passive smoke on the health of their children.

Substance Abuse

Clinicians should be alert to the signs and symptoms of alcohol and drug abuse in older children. The dangers of drugs and alcohol should be discussed with all children and adolescents, and questions about abuse should be included as part of the routine visits of older children. They should be informed about the risks of drinking and driving, the risks of dependence, the interference

with work and school, and the risky sexual behavior that often accompanies substance abuse. Programs should seek to develop social skills to resist drug and alcohol use, in addition to providing factual knowledge about such use.

Diet

All children should be encouraged to limit the daily intake of fat in their diets, especially saturated fats and cholesterol. Children should be encouraged to eat a variety of foods, especially foods high in fiber such as fruits, vegetables, grains and cereals. Adequate calcium intake should be encouraged, especially in females.

IMMUNIZATIONS

OPV and DtaP

Booster doses of OPV (Oral Polio Vaccine) and DtaP (Diphtheria, Tetanus, and acellular Pertussis) are recommended between the ages of 4 and 6. This is usually accomplished as children register for kindergarten at age 5, or for first grade.

MMR

A booster dose of MMR is recommended between the ages of 11 and 13 in order to provide more long-term immunity in those children who did not receive an earlier booster vaccine at school entry or beyond.

Hepatitis B

Hepatitis B vaccination is recommended in all children who were not vaccinated in infancy. Vaccination should begin at the first visit, with the second dose 1 month after the initial dose; and the third dose 6 months after the initial dose.

Varicella

Chickenpox vaccination should be considered for older children who have not contracted chickenpox and who have not been immunized. The greater morbidity of disease acquired during adulthood should be discussed. The dose is 0.5 cc in a one-time injection for children under 12. It is important to emphasize the risk of the disease in adulthood. It is equally important to review

the information for parents that the duration of immunity is not established, and that there is the potential need for a booster dose.

Hepatitis A

Hepatitis A vaccine is recommended for all children over the age of 2 who are in high-risk groups, especially those who are institutionalized or those traveling to endemic areas.

Pneumococcal Vaccination

This is recommended for immunocompromised children or those with chronic diseases, including pulmonary disease, cardiac disease, diabetes, asplenia, and high-risk environmental areas.

Influenza Vaccination

Influenza vaccination is recommended for residents of chronic care facilities, for children with chronic disease, including cardiac disease, pulmonary disease, metabolic diseases including diabetes, hemoglobinopathies, immunosuppression, or renal dysfunction.

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Preventive Care of the Adolescent (12–20 Years)

Marna Sternbach and Martin S. Lipsky

LEADING CAUSES OF DEATH IN ADOLESCENCE

Despite the perception that adolescents are a healthy age group, they are the only population segment in the United States with a rising mortality rate. The main causes of death in adolescence, accidents, homicide, and suicide, are largely related to adolescent risk-taking behavior and therefore preventable. Providing adolescents with guidance and specific skills in reducing their risk-taking behavior should help to decrease adolescent morbidity and mortality.

Accidents

Accidents are the leading cause of death in adolescents. The most common category is motor vehicle accidents, and fewer than 50% of teenagers wear seat belts (1). More than 40% of fatal motor vehicle crashes involve alcohol use; an additional 20% of car accidents involve drugs other than alcohol (2). Alcohol is often implicated in the second most common accidental death, drowning. At the greatest risk are adolescent males who play water sports and use alcohol. Burns, falls, poisons, and firearms are other causes of accidental deaths.

Violence

Data on interpersonal violence among adolescents are alarming. The murder rate for black males of ages 15 to 19 doubled between 1984 and 1988 to an overwhelming 78:100,000 per year (3). Gunshot wounds have become the leading cause of death in both black and white teenage boys. Because the causes and cures for violence are staggering societal issues, physicians alone have a limited role to play with individual adolescents in preventing violence; they may be more useful as adjuncts or advocates of multifaceted violence prevention programs.

Domestic abuse of adolescents is underreported (3). Unlike child abuse in general, in adolescent abuse, the victim's parents are more likely to have an above-average income and educational level. Abuse can lead to depression, substance abuse, premature sexual activity and delinquency.

Suicide

The suicide rate among adolescents in the United States has tripled in the last 30 years (4). Eighteen percent of adolescent girls and 11% of adolescent boys report attempting suicide, and more than twice as many report seriously considering suicide (5). Estimates of the prevalence of depressive disorder range from 2% to 15%. Depression may be manifested as academic difficulty, family conflict, drug or alcohol abuse, or legal trouble. Homosexual youth are at particular risk for suicide. In some studies gay and lesbian youth were two to three times more likely to attempt suicide (6).

OTHER MAJOR HEALTH RISKS IN ADOLESCENCE

Sexuality, Pregnancy, and Sexually Transmitted Diseases

Fifty percent to sixty percent of girls and seventy percent of boys will have had sexual intercourse by the time they graduate from high school (7). If current trends continue, about 40% of all teenage girls will become pregnant before they leave high school. Fifty percent of teenage pregnancies will end in abortion or miscarriage, and of those who leave high school because of pregnancy, only 40% will graduate (7). Infants of teenage mothers are at increased risk of medical complications and of child abuse.

Teenagers often use no contraception during the first episode of intercourse (and 20% of teenage pregnancies occur within a

month of that initial encounter) (8), so anticipatory guidance about methods of preventing pregnancy is important.

Sexually transmitted diseases are prevalent in adolescence: 40% of cases of gonorrhea occur in adolescents; 25% of young people with AIDS became infected during adolescence (4). Five percent to thirty percent of sexually active teenagers have chlamydia trachomatis, and 18% to 30% have HPV (7).

TOBACCO

Smoking is the leading preventable cause of death for adults in the United States. Studies have shown that if people do not begin smoking as teenagers, they are unlikely to ever smoke (9). Moreover, 85% of teenagers who smoke two cigarettes completely will become regular smokers (10). A 1992 survey showed that 70% of teenage smokers said they would not start smoking if they had the choice to make again (9).

ALCOHOL AND DRUG ABUSE

Alcohol and drugs are major risk factors in the health of adolescents. They are involved in 40% of fatal injuries in adolescents and in many homicides and suicides (11). Cocaine use contributes to violent deaths associated with illegal drug traffic, as well as to cardiac morbidity. Furthermore, illegal drug use, which affects all socioeconomic classes, is associated with family, school, and social dysfunction.

SCREENING

A complete medical history including developmental history and family history is an essential part of adolescent health maintenance. Adequate time to discuss any concerns is important. The physician should also ask specifically about sexuality (with questions directed at the appropriate stage of psychosexual development and without bias), alcohol and drugs, tobacco use, nutrition and exercise, accident prevention, and family, school, work, and social environment.

The physical examination provides a wonderful opportunity to discuss normal puberty, and to reassure and educate adolescents to be more comfortable with their bodies. While the Tanner stages may proceed at different rates, the failure to develop

breast buds in girls by age 14 or any testicular enlargement in boys by age 15 is cause for follow-up (see Chapter 34).

Breast self-examination, despite the low incidence of breast cancer in adolescence, is a practice that may be helpful to females in their future life. Teaching testicular self-examination is generally recommended for adolescent boys, especially those with a history of cryptorchidism or atrophic testes. Sexually active girls, as well as all females over 18, should have Pap smears and appropriate screening for sexually transmitted diseases. Diastolic blood pressure over 85 mm Hg and systolic blood pressure over 140 mm Hg should be followed. Scoliosis screening in schools is controversial, but should be included in the office visit (see Chapter 34). The physical examination also provides the opportunity to examine all areas of the skin for suspicious lesions and to counsel about avoiding sun exposure and protecting with sunscreen.

Routine screening of hemoglobin or Hematocrit in nonpregnant adolescents is controversial, but the American Academy of Pediatrics recommends at least one measurement for all menstruating females during adolescence. The routine measurement of serum cholesterol in adolescents is debated, but many groups recommend screening teenagers with a family history of premature cardiovascular disease or hypercholesterolemia (2).

COUNSELING ISSUES IN ADOLESCENCE

Adolescent development occurs at different rates. Early adolescents begin to separate from parents; in middle adolescence, psychologic and physical involvement with peers intensifies; in late adolescence, young people move toward involvement in intimate relationships and careers. A sense of a particular individual's place on the developmental continuum, as well as an understanding of his/her unique cultural, social, and economic context, is crucial to providing useful information and advice.

Though young adolescents usually live with their parents or guardians, and are often accompanied by them to the medical visit, confidentiality is vital in creating a trusting and open doctor-patient relationship. Physicians should ask parents to leave the room for at least part of the medical visit, as teenagers may be reluctant to discuss sensitive issues, such as sexuality or drug use, in their parents' presence. While physicians may encourage teenagers to share certain issues with their parents, they should

make clear that they will not share any confidences without their agreement. They should also clarify what may be exceptions to confidentiality, such as danger of harming themselves or others.

On the other hand, adolescents who feel connected to their families are more likely to report a general sense of well-being. Studies have shown too that in areas such as sexuality, teenagers who have discussed sexual issues with their parents were more likely to be responsible in sexual behavior (12). An authoritative parenting style, as opposed to authoritarian or permissive, has been shown to promote positive behavioral and emotional effects in adolescents. The adolescent's physician, then, can be helpful in providing education and guidance to parents, too.

Accident Prevention

Adolescents should be encouraged to use safety belts whenever they ride in a motor vehicle. They should be advised to avoid alcohol and other drugs and riding in a car driven by anyone who has been or is drinking. Physicians ought to encourage adolescents to arrange that their parents provide a ride home without recrimination if a teenager ever feels at danger riding with someone. Physicians should also promote using helmets while bicycling or roller blading.

Violence Prevention

Though violence is a complex and pervasive societal issue, and its causes are multifactorial and often debated, raising some of the issues with individual adolescents is useful. Certainly, asking directly about abuse in the family is important and necessary, given the high incidence of reported cases, and the sense that many more go unreported. Questioning adolescents about access to firearms and the danger inherent, as well as discussing ways they solve problems and potential alternatives may be helpful.

Sexuality

Physicians should create an opportunity to discuss sexual behavior in a nonjudgmental and nonthreatening way. Because of the high incidence of sexual activity in adolescence and the high rate of pregnancy, teenagers should be counseled about the health consequences of early sexual activity and the options for contraception. Some teenagers are self-conscious about using barrier

methods; some have trouble with consistent use of oral contraceptives. The advantage of both male and female condoms in protection from sexually transmitted diseases should be stressed when contraceptive options are presented.

About 10% of teenagers may be struggling with the issue of their sexual orientation. Because of society's stigmatization, they may feel isolated and depressed, often placing them at risk for suicide. Health physicians should ask open-ended questions that do not imply a particular sexual orientation. Instead of asking a teenage boy if he has a girlfriend, the physician may ask if there's anyone he feels close to, and then if this person is an emotional or sexual partner. They should also be familiar with support groups for homosexual adolescents.

Environment and Emotional Health

Inquiring specifically about each part of an adolescent's environment—home, school, work, and friends—can yield valuable information and may open issues that need to be explored. Teenagers should be asked directly about what makes them feel sad and how they deal with depressed feelings, and even if they've ever contemplated suicide.

Alcohol, Drugs, and Tobacco

Physicians should also ask directly about smoking, alcohol, and drug use. Because adolescents often do not see behavioral options open to them other than acceding to peer pressure or "just saying no," physicians can help by opening a discussion of expanded strategies. Referring teenagers to a peer support group is helpful.

Diet and Exercise

Because of the role diet plays in coronary artery disease and in cancer (colon, breast, prostate, and others), and because eating habits from childhood may persist into adult life, adolescents should be counseled about the benefits of a low-fat, high-fiber diet. Because of the high prevalence of obesity and eating disorders in adolescence, they should also be given clear guidelines about body image, caloric intake, and dieting, as appropriate.

Puberty can double the need for iron, zinc, and protein, so teenagers should also be counseled to get an adequate intake of

those nutrients (1). Guidelines for optimal calcium intake to maximize peak bone mass were recently revised upward; the current recommendation for adolescents is 1200 to 1500 mg calcium per day. Dairy products are the main and preferred source of calcium, though fortified foods (juices, breads) as well as broccoli, kale, canned fish, seeds, nuts, and various other foods also contain calcium.

Adolescents should be encouraged to engage in safe exercise on a regular basis. They should avoid heavy weight lifting and body building until their pubertal development has reached Tanner Stage 5. Those who do participate in football, weight lifting or other “power” sports should be educated about the dangers of anabolic steroids and should be discouraged from using them.

IMMUNIZATIONS AND CHEMOPROPHYLAXIS

If not previously immunized against hepatitis B, adolescents should receive the series of three shots at the initial visit, 1 month later, and 6 months later. Tetanus-diphtheria (Td) boosters should be administered at 10-year intervals. (The first Td booster is usually given at about age 5 and so the next is usually due at about age 15.) A second dose of MMR should be given in preadolescence, unless the teen already received two doses as a child. For those susceptible to chicken pox, i.e., who did not have the disease or have negative antibody titers, varicella immunization should be administered. For adolescents older than 12 years, two doses of varicella vaccine must be given, whereas those individuals less than 12 years can receive only one dose. Studies have shown that daily intake of folic acid in early pregnancy can reduce the risk of neural tube abnormalities. Therefore, teenage girls who are capable of becoming pregnant should take 0.4 mg of folate daily.

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Preventive Care of the Young Adult (20–40 Years)

Jeanne M. Ferrante

LEADING CAUSES OF DEATH IN THE YOUNG ADULT

The leading causes of death in this age group are accidents and their adverse effects, human immunodeficiency virus (HIV) infection, malignant neoplasms, diseases of the heart, and suicide (1).

Accidents and Adverse Effects

Unintentional injuries are the leading cause of death in individuals under age 45. Motor vehicle accidents account for more than half of these deaths (1). Driving under the influence of alcohol and failing to use protection devices (safety belts and motorcycle helmets) are two important behaviors that increase the risk of motor vehicle injury and death. Seat belts are 60% effective in preventing fatalities from motor vehicle accidents. Motorcycle helmets are 35% effective in preventing fatalities and 67% effective in preventing brain injuries. Currently, only about 67% of U.S. motorists use seat belts (2).

Other unintentional injuries include household and environmental injuries such as falls, drownings, fires, poisonings, suffocation, and firearm mishaps. Although motor-vehicle-related deaths decreased by 21% from 1968 to 1991, firearm-related deaths increased by 60%. By 2003, it is estimated that the number of firearm-related deaths will surpass the number of motor-vehicle deaths. Intoxication by alcohol and other drugs is involved in

40% of all fatal fires and burns and 50% of all deaths from drownings, boating mishaps, and shootings (3).

HIV Infection

HIV infection is the second leading cause of death in individuals ages 25 to 44, and the highest cause of death in males in this age group (1). (HIV is discussed in detail in Chapter 29.)

Malignant Neoplasms

Death from cancers was the third leading cause of death in individuals 25 to 44 years of age in 1992. It was the leading cause of death in females in this age group (1), with breast cancer causing the most deaths from malignancy (4). In males, leukemia was the most common cause of death from cancer before age 35. After age 35, death from lung cancer becomes the leading cause of death (5). Other cancers that can be potentially screened and prevented from progressing to invasive disease include cervical, skin, and testicular cancer.

The annual incidence of breast cancer in American women increases rapidly with age, from approximately 20 per 100,000 at age 30 to 180 per 100,000 at age 50 (see Chapter 20).

Lung cancer is the leading cause of death from cancer in males over age 35 and females over age 55. The 5-year survival rate for localized disease is only 47% and drops to 2% for distant disease (4). Cigarette smoking is the single greatest risk factor for lung cancer. Radon and asbestos, as well as environmental tobacco smoke, have also been shown to increase lung cancer risk. There is little convincing evidence that screening for lung cancer using radiography or cytology, either alone or in combination, is effective in reducing lung cancer mortality (5). In addition, there is a substantial cost to routine population testing, estimated at \$1.5 billion annually for screening chest radiographs (6). Primary prevention is therefore a more realistic strategy to reduce the morbidity and mortality from lung cancer, through prevention or cessation of cigarette smoking. Smoking caused more than 150,000 deaths from neoplasms in 1990 (7). Smoking cessation is beneficial at any age, with much greater benefits in those quitting between ages 30 and 49. An ex-smoker's risk of dying from lung cancer decreases gradually to that of nonsmokers over a period of 15 to 20 years.

In 1995, cervical cancer was diagnosed in an estimated 15,800 women, causing approximately 4,800 deaths. The 5-year survival rate is about 90% for women with localized disease and drops to about 12% for women with distant disease (4). Several studies have demonstrated an association between cervical screening programs and the reduction of morbidity and mortality from cervical cancer. This subject is also covered in Chapter 18.

Testicular cancer accounts for about 1% of all male cancers (4). Diagnostic techniques and therapeutic interventions have successfully reduced the previously high mortality of this disease. Risk factors for testicular cancer include a history of cryptorchidism, orchiopexy, and/or testicular atrophy.

Melanoma of the skin causes 3% of all cancers (5). Risk factors for skin cancer include family or personal history of skin cancer, clinical evidence of precursor lesions (e.g., dysplastic nevi, certain congenital nevi), and those with increased occupational or recreational exposure to sunlight.

Diseases of the Heart

Cardiovascular disease is the leading cause of death in the general population in the United States and the fourth leading cause of death in individuals 24 to 44 years of age (1). Although most men under the age of 35 years and women under the age of 45 years are at very low short-term risk for coronary heart disease, primary prevention of cardiovascular diseases in later years can begin ideally in this age group. High blood cholesterol, cigarette smoking, hypertension, obesity, and physical inactivity are modifiable risk factors for cardiovascular disease (see Chapters 5, 38, and 39).

Hypertension

An average reduction in diastolic blood pressure of 6 to 8 mm Hg across the population could reduce the incidence of coronary artery disease by 25% and the incidence of strokes by 50% (8). Family histories of hypertension and diabetes should be elicited in this age group and blood pressures determined at each visit, \leq yearly in previously normotensive individuals. Hypertension management is addressed in Chapter 9. Attributable risk estimates suggest that 78% of hypertension in men and 65% in women is directly attributable to adiposity. This makes weight control of

great importance for primary prevention of hypertension (8). This is dealt with in Chapters 38 and 40.

Suicide

Suicide is the fifth leading cause of death in the 25- to 44-year age group (1). Mental disorders (affective disorders and schizophrenia) and drug addiction are leading risk factors for suicide. In addition, there has been a trend of increased suicide risk in people infected with HIV and those with AIDS (9). Firearms are used in suicide by more than 60% of men, adolescents, and young adults. Alcohol intoxication is often associated (10). Drug overdose, especially with prescribed medications, such as antidepressants, is also common. Many people who commit suicide have had recent contact with medical services. Those who have attempted suicide are at a much greater risk of subsequently successfully committing suicide.

RECOMMENDATIONS FOR SCREENING IN THE YOUNG ADULT

History

A full medical and family history with particular attention to risk factors for leading causes of mortality should be obtained from all new patients and updated every 1 to 3 years. Dietary intake and amount of physical activity should be ascertained and documented. In addition, a complete sexual and substance (tobacco/alcohol/drug) use history should be obtained on all adult patients. Questionnaires such as the CAGE instrument may provide useful information on the likelihood of a previous or current problem with alcohol abuse (11). Patients at high risk for suicide should be questioned on suicidal ideations. Those suspected of suicidal intent should be questioned regarding the extent of preparatory actions and referred for further evaluation.

Physical Examination and Laboratory/Diagnostic Procedures

Recommendations are listed in Table 45.1. Desirable weights can be determined using tables of average weights (e.g., Metropolitan Life Insurance Company Table) (12). Those individuals who are obese (20% or more above desirable weight) or have a body mass index (body weight in kilograms divided by the square of height in meters) above 27.8 in men or 27.3 in women should receive appropriate nutritional and exercise counseling.

Table 45.1.**Screening physical examination and laboratory/diagnostic procedures in ages 20–40.**

Cardiovascular Screening	Cancer (CA) Screening	Screening for Infections
Height and weight (a)	Oral cavity (d)	HIV test (i)
Blood pressure	Breast examination	Gonorrhea, chlamydia, and syphilis testing (j)
Fasting total blood cholesterol (b)	Mammogram (e)	Tuberculin (PPD) skin test (k)
Fasting blood glucose (c)	Pelvic exam	
	Pap smear (f)	
	Testicular exam (g)	
	Skin exam (h)	

(a) See text

(b) At least every 5 years.

(c) In the markedly obese, persons with a family history of diabetes, or women with a history of gestational diabetes.

(d) Persons with exposure to tobacco or excessive amounts of alcohol.

(e) Women with a family history of premenopausally diagnosed breast cancer in first-degree relatives.

(f) Every 1–3 years after 3 normal annual tests.

(g) Persons at high risk for testicular CA.

(h) Persons at high risk for skin CA.

(i) Persons at high risk for HIV infection and pregnant women.

(j) Persons with multiple sexual partners.

(k) Persons at high risk for TB infection.

The U.S. Public Health Service recommends HIV counseling and voluntary testing for all pregnant women. The administration of zidovudine to HIV-infected pregnant women and their newborns has been shown to reduce the risk for perinatal transmission of HIV by approximately two-thirds (13).

COUNSELING ISSUES IN THE YOUNG ADULT

Diet and Exercise

Nutritional factors play a role in many diseases including cardiovascular disease, hypertension, obesity, many cancers including lung, colon, breast and prostate, diabetes, osteoporosis, diverticular disease, and dental disease. A diet high in whole grain cereals, vegetables, and fruits, and low in saturated fats can decrease cardiovascular events and cardiac and total death in coronary patients (see Chapter 38). Intake of red meat appears to increase the risk of colon cancer. Exercise is beneficial in improving cardiovascular

disease, hypertension, obesity, diabetes mellitus, osteoporosis, and diminished psychological well-being. A number of studies have suggested that improved cardiovascular fitness can be achieved at a lower intensity than previously thought (see Chapter 40).

Substance Use

Smoking cessation counseling should be offered on a regular basis to all patients who smoke cigarettes, pipes, or cigars, or use smokeless tobacco. Pregnant women and parents with young children should receive information on the potential harmful effects of smoking on fetal and child health. Strategies that increase the effectiveness of smoking cessation counseling are dealt with in Chapter 39.

All individuals who use alcohol should be informed of the health and injury risks associated with alcohol consumption. Consumption of alcohol should be limited to fewer than two drinks (24 ounces of beer, 10 ounces of wine, or 3 ounces of distilled spirits) per day, with special warning to those with family histories of alcoholism. Pregnant women should be advised on the harmful effects of alcohol and other drugs on the fetus. Intravenous drug users should be warned against sharing drug equipment and using unsterilized syringes and needles.

Sexual Practices

Sexually active patients should be counseled on unintended pregnancy and contraceptive options. They should also be advised that the most effective strategies to prevent infection with HIV or other sexually transmitted diseases are abstaining from sex or maintaining a mutually monogamous sexual relationship with a partner known to be uninfected. Patients who engage in sexual activity with multiple partners or with people who may be infected should be advised to use a latex condom and spermicide containing nonoxynol-9 and to avoid anal intercourse.

Injury Prevention

All patients should be counseled to use safety belts for themselves and others. Those who operate or ride bicycles or motorcycles should be advised to wear safety helmets. Smoke detectors should be installed in appropriate locations in homes, and the devices should be periodically tested to ensure proper operation. Firearm

owners should be counseled to store weapons unloaded and in a locked compartment at all times. Adults who use alcohol or other drugs should be counseled to refrain from engaging in potentially dangerous activities while intoxicated such as driving a motor vehicle, swimming, boating, handling of firearms, smoking in bed, and bicycling.

Cancer Detection

Retrospective studies of the effectiveness of breast self-examinations have produced mixed results. The U.S. Preventive Services Task Force (USPSTF) does not specifically recommend the teaching of breast self-examinations, but concludes there is insufficient evidence to recommend any change in current breast self-examination practices. Yet, this is intuitively questionable, and one study found that 44% of breast cancers were found by BSE (14). The American Academy of Family Physicians (AAFP) recommends the teaching of breast self-examination at the time of initiation of pelvic examinations.

Due to the rarity of testicular cancer in the general population, routine performance of testicular self-examination by all males would yield many false positive results. The USPSTF does not recommend for or against counseling patients to perform periodic self-examination of the testicles. The AAFP does recommend the teaching of testicular self-examinations.

Many authorities have advocated primary skin cancer prevention by limiting exposure to ultraviolet rays. Those individuals with increased occupational or recreational exposure to sunlight should be advised to apply sunscreen preparations minimally rated at 15 SPF (Sun-Protective Factor) and to wear protective clothing.

IMMUNIZATIONS AND CHEMOPROPHYLAXIS

A tetanus-diphtheria (TD) booster is recommended for all patients every 10 years. People at high risk for hepatitis B (those at high risk for HIV, recipients of blood products, and health-care workers) should be advised to receive the hepatitis B vaccine. Those people with chronic medical conditions or conditions associated with immunosuppression should be offered the Pneumococcal vaccine and yearly influenza vaccine. People born after 1956 who lack evidence of immunity to measles should be offered the measles-mumps-rubella vaccine (MMR).

Recent studies indicate that the B vitamin folic acid can reduce the risk for spina bifida and anencephaly by at least 50% when consumed daily by women before conception and during early pregnancy. The Public Health Service has recommended that all women of childbearing age who are capable of becoming pregnant consume 0.4 mg of folic acid daily. This can be obtained from multivitamins or other supplements containing folic acid and some breakfast cereals (15).

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Preventive Care of the Middle-Aged Adult (40–65 Years)

Karl E. Miller

When providing preventive health care for the 40 to 65 age group, the leading causes of mortality must be considered in order to establish preventive services. The leading causes of death in this age group are heart disease, lung cancer, cerebrovascular disease, breast cancer, colorectal cancer, and obstructive lung disease (1). Approximately 50% of all premature deaths result from unhealthy habits (2). Based on these grouped categories, preventive strategies are needed for reducing the risk factors associated with these diseases. The following includes recommendations for preventive services based on the U.S. Preventive Services Task Force (USPSTF) guidelines (3), the American Academy of Family Physicians (AAFP) periodic health examination recommendation, the American Cancer Society (ACS), and certain other groups (1). The AAFP and ACS recommendations allow for conventional wisdom. This includes the element of individual reassurance offered by a test if it be noninvasive and inexpensive, even though its cost-effectiveness may not be proved. The USPSTF takes a strict approach, endorsing only screening procedures that have been studied extensively and are proved to reduce morbidity or mortality prospectively and which satisfy the USPSTF definition of cost-effectiveness.

History

An annual updated interval and family history are recommended by the AAFP guidelines (1). These are important to establish what has transpired over the previous months in relation to patients' and their families' health risk factors. The history should include a dietary intake reviewing the percentage and types of fat the patient consumes in an average day. It should also include questions concerning the patient's physical activity. In particular, does he/she have a routine exercise program. Discussion with patients should include questions regarding tobacco products, alcohol, drug use, and sexual practices. It is important to identify risk factors in both sexes for sexually transmitted diseases and cancers. Such information determines how frequently patients are screened for preventative services.

PHYSICAL EXAMINATION

Height and Weight

The patient should have these measured on an annual basis. With routine screening, the physician can work to forestall disease processes influenced by weight increases and decreases.

Blood Pressure

Blood pressure measurements should be performed at every office visit with a minimum of one reading every 2 years.

Clinical Breast Examination (CBE)

Breast carcinoma is the number one cancer that occurs in women and the number two cause of all cancer-related deaths (4). While most physicians recommend annual CBE on all females over age 30, the USPSTF recommends that CBE should be performed annually on women starting at age 50, but allows that women younger than age 50 who have an increased risk for developing breast cancer (e.g., first-degree relative with breast cancer) may warrant clinical breast examinations on an annual basis at all adult ages. Many believe that the main benefit of the CBE at younger ages is the opportunity it presents for teaching breast self-examination (BSE) to this population. A significant proportion of breast cancers are discovered by patients.

Pelvic Examination

Routine pelvic examination is considered controversial. Most groups advocate the annual examination while performing other gynecological examinations, i.e., Papanicolaou (Pap) smears and clinical breast examinations. Other groups however, disagree with the recommendation. Because this examination can be included with the Pap smear, performing a pelvic examination with the same frequency as the patient's Pap smear is reasonable.

Digital Rectal Examination

Most groups recommend that the examination be started at age 40 in males to screen for prostate and colon cancer and age 50 in females for colorectal cancer screening. The USPSTF guidelines state that there is insufficient evidence to conclusively support the digital rectal examination (3).

Special Screens for High-Risk Patients

Patients who are classified as high risk for certain disease processes may require other portions of the physical examination. These include skin, oral cavity, thyroid, and carotid artery examinations to be covered later in this chapter.

LABORATORY AND DIAGNOSTIC PROCEDURES

There are basic laboratory and diagnostic procedures that should be performed on every patient, taking gender into consideration. These include nonfasting or fasting cholesterol, Pap smear, and mammogram. Other tests or procedures need to be performed in the high-risk groups including fasting blood glucose, screens for STDs, tuberculin skin test, hearing screen, fecal occult blood/flexible sigmoidoscopy, and electrocardiograms.

Cholesterol

The National Cholesterol Education Program (NCEP) recommends that adults have a total cholesterol every 5 years with simultaneous HDL cholesterol measurement (5). At the present time the USPSTF recommends periodic screening for fasting or nonfasting elevated cholesterol in men ages 35 to 65, and women ages 45 to 65 (3). The guidelines suggest that it may be expedi-

ent to measure cholesterol in young male, female, and elderly patients if at high risk for coronary artery disease. These risks include known coronary artery disease, family history of premature coronary artery disease, cigarette smoking, hypertension, low HDL, and diabetes mellitus. The USPSTF states that the optimal screening frequency in asymptomatic patients has not been established (3). The NCEP states if patients have two or more of the above risk factors, screening should be done annually (5).

Pap Smear

The USPSTF guidelines for Pap smears recommend that any sexually active female patient should have three annual Pap smears (1). If all three are negative, then screening can be performed every 1 to 3 years depending on the patient's risk factors. If the patient is considered low risk for cervical cancer, then screening can be performed every 3 years. If the patient has one or more of the following risk factors, she should be screened annually: sexual intercourse before age 20, multiple sex partners (more than 3), history of human papillomavirus infection, intercourse with a high-risk male partner, and smoking. A positive smoking history has a significant impact on the risk for cervical cancer and places the patient at two times the risk of a nonsmoker (6).

Mammography

The American Cancer Society's guideline for mammography is to have a baseline mammogram performed at age 35, then every other year from ages 40 to 49 and annual mammographies at the age of 50. USPSTF guidelines forego the baseline at age 35 and suggest that it may be advisable, depending on risk factors, to start mammograms at age 40 and perform them every 1 to 2 years (3). At age 50, annual mammograms are recommended. Recent studies have questioned the cost-effectiveness of mammograms before the age of 50 and cite the lack of proof that biannual mammography in the 40s lowers mortality due to breast cancer (7). Because of the effects of female hormones on the breast tissue prior to menopause, mammograms have a higher incidence of false positive results in this age group. However, recent reports suggest that mortality in the 40s could be lowered if routine mammography were to occur more frequently, e.g., \geq yearly (8). If the patient has a first-degree relative who has a positive history for breast cancer, then screening should be performed at an earlier age.

High-Risk Groups

The following represent the USPSTF guidelines for screening services for patients who are considered high risk in each of the categories.

Fasting Blood Glucose

This screen should be performed annually in asymptomatic patients who are markedly obese, have a positive family history for noninsulin-dependent diabetes mellitus, or in females, a positive history for gestational diabetes.

Screening for Sexually Transmitted Diseases

Screening can include VDRL/RPR, chlamydia testing, gonorrhea culture, and counseling and testing for HIV.

VDRL/RPR needs to be performed in prostitutes, patients with multiple partners, or who have had contact with a person with active syphilis. Chlamydia and gonorrhea screening is required in any patient who engages in prostitution, has multiple sexual partners, contact with a partner who has had multiple sexual partners, sexual contact with a partner who has an active infection, or who attends other high-risk health care facilities (e.g., adolescent and family planning clinics). The rising incidence of HIV infection in the general population requires that the physician provide counseling and testing for HIV infection in any patient who is considered high risk. The factors that place the patient at risk for HIV infection include individuals treated for sexually transmitted diseases; homosexual or bisexual males; past or present intravenous drug abuse; history of prostitution or multiple sexual partners, and females who have had past or present contact with HIV-infected, bisexual, or intravenous-drug abusing partners. Prior to obtaining blood samples for HIV screening, physicians are required to counsel patients and obtain their consent. Failure to do so can result in legal difficulties.

Tuberculin Skin Test

Over the last few years there has been a resurgence of tuberculosis (TB) (9). This has placed an increased emphasis on screening those individuals who are at risk for TB. These high-risk patients are household members of patients with active TB, individuals who are at risk for close contact with patients with active TB (e.g.,

staff members of nursing homes, dialysis units, substance abuse centers, correctional institutes, homeless shelters, and TB treatment centers), recent immigrants from countries where TB is prevalent, migrant workers, residents of nursing homes, correctional institutes, or homeless shelters, and individuals with HIV.

Hearing Screen

This screen needs to be performed in any patient who has a history of significant noise exposure, either through occupation or recreational activities. This should be done annually if the hearing risk activity is ongoing.

Colorectal Cancer Screening

Screening procedures for colorectal cancer are controversial in terms of cost-effectiveness (9). USPSTF guidelines recommend screening for all patients over age 50 (3). The guidelines state that there is insufficient evidence as to which screen is more acceptable, e.g., fecal occult blood (FOB) testing or flexible sigmoidoscopy (3). The frequency of screening suggested is annually for the FOB test and every 3 to 5 years for flexible sigmoidoscopy combined with the FOB. The American Cancer Society recommends that every patient over the age of 40 receive annual digital rectal examination and for those over 50 annual rectal examination and FOB and flexible sigmoidoscopy every 3 to 5 years, over two consecutive years. If these are negative, then screening can be performed every 3 to 5 years, depending on risk factors. Most gastroenterologists recommend a colonoscopy every 3 years starting at age 50 for those patients who have a first-degree relative with colon cancer, colon polyps, or cancer family syndrome (3). Familial adenomatous colon polyposis leads to cancer in all afflicted individuals by the age of 40 and does not fall into the realm of screening. The greatest challenge is improving patient compliance with these recommendations.

Counseling

According to the AAFP guidelines, one of the most effective tools available for reducing morbidity and mortality in the United States for physicians to address personal health practices of their patients. Counseling patients with regard to diet and exercise, substance abuse, sexual practices, injury prevention, dental

health, and other measures is more effective than any other intervention (1).

Diet

The average American consumes more calories, particularly in fat, than what is needed for basic nutrition. Discussions with patients should include assessments of their daily dietary intake of fats, and particularly, an assessment of the amount of saturated fats consumed (see Chapter 38).

Exercise. The vast majority of Americans in this age group lead a sedentary lifestyle, carrying with it increasing risk of coronary artery disease, diabetes, hypertension, and osteoporosis. AAFP guidelines recommend that all patients receive counseling concerning a regular exercise program (1) (see Chapter 40).

Substance Abuse

Some of the leading causes of preventable deaths in the United States occur secondary to substance abuse. In this area, physicians have tremendous impact on cessation rates, but studies show that few use those skills to assist their patients with high-risk behaviors such as substance abuse (10).

AAFP guidelines indicate that all patients in this age group should receive routine queries concerning alcohol use (1). They should be asked to describe the quantity consumed, the frequency of consumption, and questions concerning impairment issues. Positive answers to any two items of the CAGE questionnaire may indicate alcohol abuse (11). 1. Have you ever felt you should *cut down* on your drinking? 2. Have people *annoyed* you by criticizing your drinking? 3. Have you ever felt bad or *guilty* about your drinking? 4. Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (*eye-opener*)? As in smoking cessation, physician counseling can have an influence on the patient who abuses any substance, particularly at an early age. If a patient has a positive history for substance abuse, counseling services and treatment options need to be discussed and plans established with the patient to address the abuse problem. Also, if patients have a positive history of substance abuse, operating automobiles and other equipment while impaired must be addressed. Information concerning designated drivers and other options should be provided for these individuals.

Tobacco Cessation

Each year approximately 430,000 people die prematurely as a result of tobacco use. Thus, smoking cessation is the single most important issue when counseling patients concerning their health habits. Even simple interventions can lead to modest long-term quit rates, with more intensive interventions leading to much higher rates. (Chapter 39 deals with techniques employed in smoking cessation.)

Sexual Practices

Issues such as partner selection, use of condoms for safer sex, and the risks associated with anal intercourse need to be addressed in a frank, open approach. Other major issues facing this age group with regard to sexual practices are unintended pregnancies and contraceptive options. The majority of the patients in this group have completed their families and have no further interest in becoming parents. It is at this time that physicians need to discuss permanent sterilization (bilateral salpingectomy or vasectomy) as an option for contraception. Prior to a patient making this decision, it is important to evaluate the patient's motivation and to establish that this is the best option.

Injury Prevention

Declining incidence of injuries in this age group notwithstanding, issues to be raised include the use of seat belts, safety helmets, smoke detectors, and smoking near bedding or upholstery. Patients at risk for back injuries include those with previous back injuries, body configuration with abdominal adiposity, and who participate in activities that place them at risk for back injuries. These individuals must be counseled regarding the appropriate technique for lifting, bending, and twisting in order to reduce the potential for back injuries that could result in a loss of function.

Dental Health

Discussed in detail in Chapter 2.

IMMUNIZATIONS AND CHEMOPROPHYLAXIS

In a recent study, the rate of immunizations for adults demonstrated rates of compliance of less than 30% for tetanus-diphtheria, influenza, and pneumococcal vaccinations (12). Patient-related compliance issues may include obliviousness and hesitancy

due to concerns about adverse reactions. Physician issues include oversight, particularly of specific indications based on patients' lifestyles and occupations. Another issue facing physicians is that many patient office visits are for acute care when immunization status is not often addressed. Further, many of the adult immunizations are not covered by insurance plans, and many adults lack convenient access to these services. It is imperative that physicians address immunizations in their adult patients and assist in reducing the barriers that they face with regard to obtaining the appropriate immunizations.

Tetanus-Diphtheria (Td) Booster

Tetanus and diphtheria can be controlled by following routine guidelines for immunization (12). First, one establishes the approximate date of the patient's last immunization and whether he or she has had at least three doses. Routine immunization should be performed every 10 years except in event of wounds or other injuries. If the patient has had at least three doses of tetanus and the wound is clean and minor, a Td booster is only indicated if the last booster was more than 10 years ago. If the wound is contaminated with dirt, feces or saliva, consists of a puncture or missile injury, or is the result of a crush, burn or frostbite, a Td booster is indicated for patients whose last Td booster was more than 5 years ago. With patients who are uncertain of any Td immunizations or have had less than three doses, tetanus immune globulin should be administered as well.

Hepatitis B Vaccination

USPSTF guidelines for hepatitis B recommend immunization only for patients at risk for contact with individuals with hepatitis B (3). These high-risk patients include health-care workers, recipients of some blood products, homosexually and bisexually active males, intravenous drug users, household and sexual contacts of patients with active disease, prostitutes, and patients who have a history of multiple sex partners.

Influenza Vaccine

In this age group, the AAFP guidelines recommend immunization of patients who are at high risk for significant morbidity and/or mortality from this viral infection (1). These include, in particular, those who have chronic cardiovascular, pulmonary,

renal, metabolic, or immunosuppressive diseases (13). The vaccine is also recommended for those individuals who can transmit the virus to this high-risk group such as health-care workers and household contacts. In addition, to reduce risks of influenza epidemics in crowded environments such as nursing homes and other chronic care facilities, immunizations are recommended for residents. The optimal time for immunization is from mid-October to mid-November. Protection against influenza occurs approximately 2 weeks after vaccination (13).

Pneumococcal Vaccine

Immunization with pneumococcal vaccine is recommended for those patients who are predisposed to pneumococcal disease, and for those who are immunosuppressed. The medical conditions that increase the chances of significant morbidity and mortality with pneumococcal disease include chronic cardiovascular, pulmonary, metabolic, and liver disease. Immunosuppressed patients who are at risk include those with HIV, an organ transplant, lymphoma, renal failure, and asplenia (either surgically removed or functional as in sickle cell disease) (13).

Other Concerns

Physicians also need to be alert for any signs or symptoms of the following: depression, suicide risks, physical abuse or neglect, malignant skin lesions, and peripheral artery disease (1).

Depression

Major depressive disorders occur in more than 6 million Americans per year, many of whose cases go unrecognized by their primary-care physicians (14). Risk factors of depression include previous depressed episodes, positive family history for depression, previous suicide attempt(s), female sex, medical comorbidity, lack of social support, stressful life events, personal history of sexual abuse, and current substance abuse (1).

Suicide Risk Factors

Risk factors include recent divorce or separation, unemployment, depression, alcohol or substance abuse, serious medical illnesses, recent bereavement, and living alone. An interval social history with patients is vital in order to assess these risk factors.

Domestic Violence

The amount of domestic violence is grossly under-reported by the medical community (15). Victims come from any socioeconomic, educational, or racial group. It is important to maintain an index of suspicion for domestic violence in patients who report mechanisms of injuries that are inconsistent with physical findings, or in a patient whose live-in partner will not allow a private discussion of the injuries between the doctor. In this situation, physicians need to be able to provide support for the patients and assist them in understanding their options. If a patient is involved in an abusive relationship, it is vital to assess his/her immediate safety, homicidal threats and suicidal ideation, intent and plans. If she is in immediate danger, an escape plan must be discussed, including having the phone numbers of police and victim hot lines, leaving packed suitcases at a friend's or family member's home, and a plan for the patients and children to escape prior to the onset of violence. Physicians also need to refer these patients to counseling services in order to assist patients in moving from denial to acknowledgment of the situation and working toward a solution.

Malignant Skin Lesions

Patients who have had an outdoor occupation, severe sunburn at a young age, fair hair and skin, or who have a personal or family history of skin cancer need to be assessed on a routine basis (1). Also, these patients must be informed of the need to use sunscreen when there is the potential for sun exposure.

Peripheral Artery Disease

Routine screens should be performed in those patients who are over age 50, who smoke, or have diabetes mellitus (1). This would include peripheral pulses and an assessment of capillary refill. Routine screening consists of eliciting history of claudication and checking peripheral pulses for palpability.

Summary

It is vital to establish a preventive plan for each patient including all the services indicated in this chapter. Physicians need to organize plans based on an assessment of the patients' risk factors and what preventive services are thus indicated. The goal is to maintain a

healthy lifestyle in this age group in order to delay the more common medical illness that impact this group.

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Preventive Care of the Older Adult (>65 Years)

Michael H. Bross and Ames F. Tryon

Preventive care of the elderly patient, age 65 or greater, may be divided into primary, secondary, and tertiary interventions (1, 2).

PRIMARY PREVENTION

Immunizations

Annual influenza vaccine is recommended in the fall. Pneumococcal vaccine is generally given once per lifetime but may be safely repeated, after 6 years, for high-risk elderly patients (3). The tetanus-diphtheria (Td) vaccine is recommended every 10 years.

Nutrition

It is estimated that more than 30% of elderly people living in the community consume diets that are deficient in at least one major nutrient. Furthermore, approximately 17% of persons over age 65 consume less than 1000 calories per day. In addition, the fluid intake of many elderly is below acceptable levels. Problems of malnutrition and dehydration are more common than would be expected in a modern western society. Causes of nutritional deficits include impaired mental status, isolation and immobility, loneliness, poor oral health status, and environmental inadequacies.

A healthy diet includes fruits, vegetables, and grain products high in fiber. Limited intake of fat (less than 30% of total calories) and cholesterol (less than 300 mg/day) can be maintained with lean meats, fish, and poultry. Calcium supplementation is

usually necessary to achieve the recommended 1500 mg/day elemental calcium.

Exercise Programs

Aerobic exercise and weight-lifting programs initiated in later life have numerous physiologic benefits. Strength and coordination are increased; systolic blood pressure and total peripheral resistance are decreased, with an increase in cardiac output and maximal oxygen consumption. Cholesterol, triglycerides, and weight fall as the metabolic rate increases. The relative risks of stroke, myocardial infarction, and osteoporosis are improved.

Nevertheless, it is difficult to motivate the sedentary older patient to begin a new lifestyle. Presenting a variety of activities may help to elicit and maintain patient interest. These include dance, yoga, swimming, golf, tennis, cycling, gardening, weight lifting, and walking. Walking 4 to 7 days per week significantly delays the onset of disability in both blacks and whites over age 70 (4).

Psychosocial History

Success in care of the elderly often depends upon a clear understanding of the psychological and mental health status of the patient and the social background. Assessment includes a focus on socialization patterns and support networks, including the availability of competent caregivers.

Injury Prevention

The three most common causes of injuries in the elderly are falls, motor vehicle accidents, and burns. The most common risk factors for falls are postural hypotension, medications, abnormal vision and hearing, decreased mobility and gait disturbances, decreased mental status, previous history of a fall, decreased ability to perform more than two of the activities of daily living, serious cardiovascular and neurological diseases, and alcohol use. For high-risk elderly patients, home-based multifactorial interventions are helpful to reduce falls.

Many of the risk factors related to falls are also implicated in motor vehicle accidents. Patients with cognitive impairments, cardiovascular disease, fluctuating mental status, and gait instability are at very high risk, as are patients with decreased visual thresholds and impaired peripheral vision. It is often advisable to

recommend periodic retesting of driving skills. Patients should be counseled to use seat belts and avoid driving under the influence of alcohol or drugs.

Finally, due to the same causes, older people are at high risk for burns. An environmental analysis of the home is often helpful in reducing risks, for the purpose of reducing hot water temperature to <120 to 130°F and assuring proper functioning of appliances and lighting.

SECONDARY PREVENTION

Vital Signs

Blood pressure, temperature, pulse, respiratory rate, and weight are recorded at each visit.

Hypertension affects more than 40% of the elderly. Non-pharmacological and/or pharmacological treatment of repeated systolic pressure over 160 mm Hg (5) and/or diastolic pressure over 90 mm Hg is indicated. Chapter 9, using Joint National Commission guidelines, defines hypertension as 140/90.

Temperature elevation or significant change in pulse, respiratory rate, or weight may be the sole evidence of serious illness. Periodic measurement of height and weight helps to diagnose obesity, malnutrition, and osteoporosis.

Colorectal Cancer

Annual fecal occult blood testing and/or sigmoidoscopy every 3 to 5 years are recommended for those over 50 years (6). The 60-cm flexible sigmoidoscope is more sensitive and better tolerated than rigid sigmoidoscopy. For those with first-degree family histories of colon cancer or polyps, many would recommend colonoscopy on the same schedule.

Breast Cancer

Annual clinical breast examination and mammography every 1 to 2 years are indicated to age 70. Further screening to age 75 may be beneficial in women with reasonable life expectancy.

Cervical Cancer

Pap smear is indicated every 1 to 3 years unless the patient has documentation of several normal Pap tests. After three normal

screens, Pap smears may be stopped. Pap smears may also be stopped after hysterectomy for nonmalignant disease. If a hysterectomy was performed for cervical malignancy, Pap smears should be repeated every 1 to 3 years.

Lifestyle

Smoking cessation is important at any age and reduces morbidity and mortality. Use of smokeless tobacco should also be discouraged due to its association with oral cancer. Counseling directed at smoking cessation, community programs, and medication therapy are often helpful.

Screening for alcohol abuse can be done with a detailed history of alcohol use and/or a standardized screening questionnaire. The CAGE questionnaire (7) consists of four questions: 1) Have you ever felt you should *cut* down? 2) Have others *annoyed* you by criticizing your drinking? 3) Have you ever felt *guilty* about your drinking? and 4) Have you ever needed an *eye opener* in the morning? Any positive answer merits further investigation; two or more positive answers is strongly suggestive of alcoholism. Alcohol-dependent patients should be referred to appropriate treatment programs.

The sexual history is an often neglected portion of geriatric care. Absence of sexual activity often results in patient or marital distress, requiring further investigation for correctable causes. The physician may counsel patients to avoid high-risk sexual practices and offer testing for sexually transmitted diseases.

Iatrogenic Effects

It is estimated that nearly one-third of elderly patients report adverse drug reaction due to prescribed drugs or a combination of prescribed and over-the-counter medications. Furthermore, a significant number of older patients suffer physical and emotional stress after discharge from the hospital. Adequate discharge planning and continuity of care efforts will help reduce iatrogenic effects. Asking patients to bring all medications, both prescription and over-the-counter, to each clinic visit. The "brown bag" test allows the physician to review the medications, and to compare medication record with each patient's practices.

Foot Care

The feet must be assessed for color, temperature, pulses, pressure points, and fungal infection. Elderly patients often need assistance with nail trimming, proper hygiene, and adequate footwear. Venous insufficiency, arterial insufficiency, and peripheral neuropathy can be addressed, decreasing skin breakdown and ulceration.

Postmenopausal Estrogen Therapy

This is addressed in Chapter 19.

Urinary Incontinence

Urinary incontinence affects more than 20% of the elderly and may result in social isolation, depression, and increasing dependence. This problem is addressed in detail in Chapter 17.

Hearing Loss

This is a frequent serious social problem for the elderly. Hearing loss is dealt with in Chapter 1. The physician can do a great service by 1) speaking more slowly rather than louder to the aged person with sensorineural loss; 2) instructing the patient's family and friends to do likewise, and 3) referring appropriately for hearing aids.

Vision Loss

Visual acuity can be periodically screened with a Snellen eye chart at 20 feet. Corrective lenses should be used, if available. Patients with visual acuity worse than 20/40, and patients with impaired function from poor vision, often benefit from ophthalmologic referral. All diabetics should be referred to an ophthalmologist yearly.

Arthritis

More than 45% of the population over age 65 suffer from arthritis. Secondary prevention of arthritis is critical to prevent serious disability. Accurate diagnosis of the underlying etiology allows the clinician to begin appropriate medication to control inflammation

and pain. Physical and occupational therapy can provide expertise regarding activity, rest, exercise, protective splinting, home modification, and the activities of daily living (ADLs) (8). For example, wearing elastic gloves at night and avoiding excessive twisting of the fingers can markedly decrease the edema and deformities of arthritis involving the hands.

Diabetes Mellitus

Diabetes mellitus affects approximately 15% of the elderly and is the most common etiology of end-stage renal failure. Annual screening for proteinuria and measurement of serum creatinine can detect the onset of diabetic nephropathy. A reduction in blood pressure to approximately 130/85 mm Hg slows the rate of diabetic nephropathy. In addition, treatment of hypertension with an angiotensin converting enzyme (ACE) inhibitor medication further slows the progression of diabetic nephropathy. In normotensive diabetic patients with proteinuria (microscopic or greater), ACE inhibitor therapy is beneficial in slowing nephropathy. Moderate restriction of dietary protein, to 0.6 to 0.8 g per kg per day, may be of benefit in early nephropathy. Rapidly progressive and advanced renal failure warrant nephrology consultation. This is addressed in more detail in Chapter 31.

Tight glycemic control is risky in the elderly. Potential benefits to end organs must be weighed against the risks of hypoglycemia on an individual basis. To help preserve vision, yearly ophthalmology referral is indicated.

Cognitive Impairment

The prevalence of dementia rises sharply with age, from approximately 5% of the population at age 65 to 20% of the population at age 80. Delirium, the sudden change in consciousness resulting from an organic factor, also occurs much more often with advancing age. When an elderly patient presents with declining function or suspected mental status change, the Mini-Mental State examination (9) or the Short Portable Mental Status Questionnaire (10) can be used to screen for cognitive impairment. Educational and cultural background must be considered when interpreting screening tests. Abnormal screening tests warrant full evaluation and treatment (see Chapter 10).

Depression

Screening for depression is indicated when the patient presents with a flat or sad affect or with many confusing somatic symptoms. The Yesavage Geriatric Depression Scale (11) is a screening test that can be quickly completed by the patient. A positive screening should be followed by a full mental status examination. Successful treatment of depression helps preserve quality of life and independence (see Chapter 50).

Mobility Assessment

Elderly individuals who suffer acute episodes or who have chronic disease often exhibit decline in functional status. Ongoing assessments of the ability of older patients to perform the activities of daily living (ADLs) (8), as well as the instrumental activities of daily living (IADLs) (12), are essential to effective elder care. The activities of daily living include the ability to bath, dress, use the toilet, transfer from place to place, remain continent, and feed oneself. The instrumental activities of daily living include the ability to use a telephone, shop for groceries, prepare meals, do housekeeping, laundry, use public transportation where available, take medications, and handle finances. Once the clinician recognizes difficulties, rehabilitation and the proper level of assistance can be arranged.

Atherosclerotic Diseases

Heart

In patients with unstable angina or a history of myocardial infarction, daily use of aspirin and a beta-adrenergic blocker can lower mortality rates. Contraindications to beta-adrenergic blocker therapy include systolic heart failure, insulin-dependent diabetes mellitus, and severe pulmonary disease. In patients with left ventricular systolic dysfunction, indicated by an ejection fraction of less than 40 %, ACE inhibitor treatment is beneficial.

Cerebrovascular Disease

This concerns transient ischemic attacks and strokes. They are dealt with in detail in Chapter 7.

TERTIARY PREVENTION

Victimization and Abuse

Approximately 1.1 million elderly people in the United States may be victims of abuse each year. Categories of abuse in this population include material and financial; physical; sexual; and psychological/emotional. In addition, older people are often subject to passive neglect due to caregivers' lack of knowledge and/or commitment. Active neglect occurs when caregivers know what to do but fail to carry out effective action plans. Practitioners should be aware that the abuser is usually a relative, most commonly the spouse. When signs and symptoms of abuse are recognized, intervention strategies should be employed.

Severe Mental Illness

Dementia is the most prevalent form of severe mental illness and is typically progressive. Correct diagnosis of the underlying etiology is essential for proper medical treatment and disposition. Depression, schizophrenia, and other types of severe mental illness may masquerade as dementia and may be responsive to psychiatric interventions. Old records, psychiatric consultation, and medication trials are often helpful in patient management.

Advanced behavioral, cognitive, and dependency problems require constant care. The physician, along with the social worker, can help arrange the appropriate level of care. Family member burn-out may be alleviated by respite programs, home health programs, adult day-care, and support groups. When the need for institutional care is anticipated, it is best to make the necessary arrangements before a crisis occurs.

Extreme Physical Debility

The end-stage of many diseases is a bedridden state. Bedridden patients are subject to urinary and fecal incontinence, decubitus ulcers, muscle atrophy, joint contractures, pneumonia, urinary infections, sensory deprivation, and many other complications. A multidisciplinary team can best address the numerous needs of extreme debility. Physical and occupational therapists can teach the patient (and caregivers) exercises, transfer maneuvers, and other means of maximizing physical function. Ongoing nursing care is vital to monitor diseases, prevent skin breakdown, address incontinence, insure proper medications, and perform other

skilled care. Dietitians, pharmacists, social workers, and other health-care professionals compose a health-care team that can work together to help meet additional needs of physical debility.

Advance Directives

Elderly patients and their caregivers and/or family members should be counseled on the need for preparing wills, trust agreements, living wills, and durable powers of attorney for health care. Most states have specific statutes concerning the preparation of living wills and durable power documents. While legal counsel is often helpful, individual patients can use available forms to prepare their own documents.

CONCLUSION

The average family physician encounter is approximately 15 minutes. Preventive health measures therefore require several visits to be accomplished. Practice studies have found that using flow charts and assigning a staff member for preventive medicine education improve the delivery of preventive services. The patient must be recognized as the most important part of the decision making process.

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Travel Medicine

Zvi Gross and David R. Rudy

INTRODUCTION

Of 30 million Americans who travel abroad each year, 8 million go to developing countries with high incidences of tropical and infectious diseases. Travelers to lesser developed areas for 1 month have a 60% overall chance of becoming ill and nearly 1% chance of being admitted to the hospital. Travelers' diarrhea is the most common medical problem, while malaria and viral hepatitis are the most important diseases to be avoided overseas. Other commonly acquired illnesses include viral syndromes, URI, skin rashes and sunburn, otitis, sprains, contusions, and superficial injuries. In 1984, 1298 travelers' deaths occurred, mainly due to cardiovascular events, plus traffic and swimming accidents, often involving alcohol. Multiple factors influence the individual risk: region and duration of visit, use of prophylactic measures, and traveler's health status. Most travel-related diseases can be prevented or treated early if properly diagnosed. Table 48.1 classifies categories of travel by degree of risk.

Pretravel Consultation

Travelers' clinics of varying levels of function exist, which provide travel and health advice, administer vaccines, including the authorized yellow fever vaccine, prescribe related medications. Some treat tropical diseases. Otherwise, patients may be referred to the following sources of travel information:

1. Center for Disease Control and Prevention
2. Public Health Service

Table 48.1.
Individual risk assessment.

By Country

1. Africa	3
2. India	2
3. South America	3
4. North America	1
5. Central America	2
6. Asia	2
7. Caribbean	1
Haiti	2
8. Europe	1
9. New Independent States	2
10. Pacific Islands	2

By Itinerary

1. Trekking and backpacking, no day-to-day plans	3
2. Camping and rural travel	3
3. Youth hostel, elder hostel, outdoor activities	3
4. Staying with family, small hotels, safari	2
5. Major resorts, day trips, structured itinerary	1
6. Cruise ship with guided day trips	0
7. Mission work, hospital or physical labor	2

Length of Stay

1. 1–3 weeks	1
2. 4–8 weeks	2
3. 3–6 months	3
4. 6 or more months	3

General Health and Age of Traveler

1. <5 years of age	1
2. >65 years of age, add 1 for every 5 years	
3. Altered immune status, add 2	
4. For every diagnosis code for chronic illness, add 1	
5. For pregnancy, add 1	

Scoring in Terms of Potential Health Risks to Traveler

1–5, Very little risk, recommended vaccines, TD and water precautions.

6–7, Moderate risk, in addition to above, may need instructions about specific health problems or health risks within the country traveled.

>8, Travel could be dangerous without above instructions, plus list of safe clinics in area traveled, as well as pre- and post-travel physical examinations. Traveler could be at great risk of becoming ill.

All travelers should be cautioned about the risk of accidents (automobile and pedestrian). Accidents are the leading cause of death in people traveling out of the country. Pickpockets, muggings, rapes, terrorist attacks, and civil disturbances are all becoming more frequent occurrences out of the country to the unwary traveler who gets separated from the group.

3. Travelers' Clinics

4. International Travel Health Guide (1)

The following may be addressed during a pretravel visit (6 to 10 weeks beforehand):

- a. Review of the itinerary to plan for preventive measures.
- b. Review of the medical history and medication.
- c. Discussion of immunization recommendations, their side effects, and administration thereof.
- d. Review of measures to prevent traveler's diarrhea, hepatitis A–E, STDs, motion sickness, jet lag, ear and sinus diseases, travelers' thrombosis, mountain sickness, and diseases caused by mosquito and insect bite.
- e. Prescription of medication to prevent and treat the above.
- f. Agreement to provide telephone consultation and/or help with referral to foreign physicians.
- g. Tuberculosis screening as baseline.
- h. Recommending dental check-up and an extra pair of glasses with their prescription.
- i. Discussion of preventive measures against accident, crime, and political instability.

Traveling with Medical Problems

The following are hints relevant to common pre-existing conditions.

Heart Disease

Travel contraindications include severe angina, uncontrolled hypertension (HTN), symptomatic heart failure (CHF), and <4 weeks postmyocardial infarction (MI).

Lung Disease

Air travel is considered safe if ambulating one block or one flight of stairs produces no dyspnea.

Diabetes Mellitus

Medication and supplies should be sufficient to last the entire trip.

Diabetic flight menu should be arranged 72 hours before departure.

Oral hypoglycemics to be taken according to the local time. Insulin-dependent diabetics should have personal glucose monitoring (e.g., Accuchecks) every 6 hours or ac during flight.

Insulin adjustments:

East Bound

Single dose: Usual dose on the day of departure. $2/3$ usual dose on the first morning at destination. Remaining $1/3$ AM dose for glucose over 240, 10 hours after morning dose. Usual dose on the second day at destination.

Two doses: Usual doses on the day of departure. $2/3$ usual dose on the first morning at destination. Usual evening dose 10 hours after AM dose. Remaining $1/3$ AM dose for glucose over 240, 10 hours after AM dose. Usual dose on the second day at destination.

West Bound

Both regimens: Usual dose on the day of departure. $1/3$ usual AM dose for glucose over 240, 18 hours after AM dose, followed by a snack. Usual dose on the first day at destination.

Peptic Ulcer Disease

H₂ blockers increase the risk of travelers' diarrhea. Carafate may be considered as an alternative and may even reduce the chance of diarrhea.

Drug Interactions

Mefloquine (Lariam) and beta blockers or calcium channel blockers or quinines may cause heart block and dysrhythmias. Ciprofloxacin may increase levels of warfarin and theophylline. Antacids and carafate may decrease absorption of quinolones.

Immunization

Review immunization requirements 8 to 10 weeks prior to departure (Tables 48.2 and 48.3).

Routine immunization should be up to date.

Influenza vaccine is recommended.

Recommended for developing countries destination: 1) Td booster if not administered within 5 years; 2) measles booster if born after 1956; 3) polio booster; 4) immune globulin; 5) typhoid fever vaccine.

For travel on a short notice, the traveler should have an accelerated immunization schedule.

Table 48.2.
Immunizations recommended for world travel.

	Diph-Tet	Polio	Japan Enceph	Yel-Fev	Mening	Rabies	Hepa-B	Hepa-A	Typhoid	Influenza
Algeria	×	×				×	×	×	×	×
Benin Rep	×	×				×	×	×	×	×
Bermuda	×	×								
Bolivia	×	×		×		×	×	×	×	×
Brazil	×	×		×		×	×	×	×	×
Burkina Faso	×	×		×		×	×	×	×	×
Ca	×	×		×		×	×	×	×	×
Caribbean Isl.	×	×								
China	×	×	×			×	×	×	×	×
Colombia	×	×		×		×	×	×	×	×
Ivory coast	×	×		×		×	×	×	×	×
Djibouti	×	×		×		×	×	×	×	×
Dom. Rep.	×	×				×	×	×	×	×
Ecuador	×	×		×		×	×	×	×	×
Egypt		×				×	×	×	×	×
French Gina	×	×		×		×	×	×	×	×
Gabon	×	×		×		×	×	×	×	×
Guatemala	×	×				×	×	×	×	×
Haiti	×	×				×	×	×	×	×
India	×	×	×		×	×	×	×	×	×
Indonesia	×	×	×			×	×	×	×	×
Israel Mideast	×	×				×	×	×	×	×
Kenya	×	×		×		×	×	×	×	×

Table 48.2 (continued).
Immunizations recommended for world travel.

	Diph-Tet	Polio	Japan Enceph	Yel-Fev	Mening	Rabies	Hepa-B	Hepa-A	Typhoid	Influenza
Laos	X	X	X			X	X	X	X	X
Madagascar	X	X				X	X	X	X	X
Malaysia	X	X	X			X	X	X	X	X
Malidiv E Isl	X	X				X	X	X	X	X
Mali	X	X		X*	X	X	X	X	X	X
Mauritius	X	X				X	X	X	X	X
Mexico	X	X			X	X	X	X	X	X
Morocco	X	X				X	X	X	X	X
Myanmar	X	X	X			X	X	X	X	X
Nepal	X	X			X	X	X	X	X	X
Nigeria	X	X		X*		X	X	X	X	X
Pakistan	X	X	X			X	X	X	X	X
Peru	X	X		X*		X	X	X	X	X
Philippines	X	X	X			X	X	X	X	X
South Africa	X	X				X	X	X	X	X
Saudi Arabia	X	X			X*	X	X	X	X	X
Senegal	X	X		X*	X	X	X	X	X	X
Seychelles	X	X				X	X	X	X	X
Sierra Leone	X	X		X*	X	X	X	X	X	X
Sri Lanka	X	X	X			X	X	X	X	X
Thailand	X	X	X			X	X	X	X	X
Togo	X	X		X*	X	X	X	X	X	X
Tanzania	X	X		X*	X	X	X	X	X	X

**Table 48.2 (continued).
Immunizations recommended for world travel.**

	Diph-Tet	Polio	Japan Enceph	Yel-Fev	Mening	Rabies	Hepa-B	Hepa-A	Typhoid	Influenza
Turkey	X	X				X	X	X	X	X
Venezuela	X	X		X*		X	X	X	X	X
Vietnam	X	X	X			X	X	X	X	X
Cambodia	X	X	X			X	X	X	X	X

x* Entry or exit to this country may be denied if proof of this vaccination is not presented.

Routine immunizations such as DT, MMR, polio, should be kept up to date as a matter of routine.

The status of cholera epidemics is available by contacting the CDC in Atlanta, (404)332-4559.

There is some confusion about the necessity of cholera vaccine among health professionals, as well as the traveling public. While the cholera vaccine is less than 50% effective in reducing *Vibrio cholera* O1 infection, and probably totally ineffective in the case of *Vibrio cholera* O-group, some countries will still demand proof of vaccination for this disease. In that case, usually one shot within the past 6 months will satisfy their requirements. The primary series, two shots, need never be repeated; a booster will suffice.

In recent years, individuals making their religious pilgrimage to Mecca must have a recent dose of cholera vaccine as well as a dose of meningococcal vaccine or risk being vaccinated as they leave the plane in Saudi Arabia. Documentation in the form of an International Certificate of Vaccination should be filled out and stamped with an official vaccination stamp and stapled to their current passports.

Simultaneous administration of other vaccines and medications in addition to special health concerns should be followed according to the manufacturer's recommendations or using guidelines listed in Health Information For International Travel (HHS Publication No. (CDC) 95-8280), available for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington DC 20402, (202) 512-1800.

Certain uncommon vaccines are not necessary for the casual traveler, such as Japanese encephalitis and pre-exposure rabies. These are usually given to those individuals who are at risk as indicated in the Health Information For International Travel, or as recommended by the manufacturer.

Those who are frequent out-of-country travelers should consider the hepatitis B vaccine, since there is a greater chance of infection through medical care or sexual activity in the longer trips.

Reprinted from: Rose SR. International Health Guide. 6th ed. Northampton, MA: Travel Medicine, Inc.

Contributed by Linda Shearer, LPN, Ohio State University Travel and Immunization Clinic.

Table 48.3.
Suggested scheduling of predeparture vaccinations.

Weeks to Departure	Immunization
12 weeks (or before)	Update all routine immunizations, as necessary (tetanus, diphtheria, polio, measles)
8–10 weeks	First hepatitis B (Engerix-B), first typhoid (if receiving the injectable vaccine), first Japanese encephalitis (JE)
6–8 weeks	Yellow fever, first rabies, second JE
5–6 weeks	Second rabies, meningitis, cholera
3–4 weeks	Second typhoid, second hepatitis B, third JE, hepatitis A, oral typhoid series (if injectable vaccine not used)
1–2 weeks	Immune globulin (IG), third rabies, third hepatitis B

- If time is short, immune globulin (IG), as well as most vaccines, can be given simultaneously, or over a period of a few days.
- Live virus vaccines (MMR, OPV, yellow fever) should be given either on the same day, or separated by at least 1 month.
- Immune globulin should be given at least 2 weeks after MMR.
- Separate yellow fever and cholera by three weeks, or administer on same day.
- Don't get injectable typhoid and cholera shots on the same day, or in the same arm.
- Oral polio vaccine (OPV) should be taken on the same day as oral typhoid vaccine (OTV); OPV can be given 7–10 days before or 10–14 days after OTV.
- If necessary, rabies and JE can be given on an accelerated schedule of 2 IM doses, given 1 week apart.
- Wait 3 weeks after intradermally administered rabies vaccine to start chloroquine; get IM rabies vaccine if 3-week interval not possible.

Reprinted from Rose SR. International travel health guide. 6th ed. Northampton, MA: Travel Medicine, Inc., 1995:24.

Yellow fever vaccine is not required but recommended for developing countries.

Cholera vaccine is required but only partially effective (see Table 48.1 legend).

No vaccinations are required to re-enter the United States or Canada.

Malaria Prophylaxis

Pophylaxis is strongly recommended for travelers to endemic areas. Only four plasmodium species infect humans: *P. vivax*, *P. falciparum*, *P. ovale*, and *P. malaria*. *P. vivax* and *P. falciparum* are responsible for most illnesses and both may be chloroquine resistant. *P. falciparum* is the most dangerous form of malaria.

Chloroquine is the drug of choice for the susceptible plasmodium and is well-tolerated when taken with meals.

Chloroquine phosphate 500 mg or 300 mg base weekly is given 1 week before arrival and 4 weeks after departure from an endemic area. Rarely, chloroquine causes dizziness, headache, blurred vision, and itching. For chloroquine-resistant plasmodium mefloquine (Lariam) 250 mg is given weekly. This starts 2 weeks before arrival in order to monitor potential side effects, and continues for 4 weeks after leaving an endemic area. Mefloquine is contraindicated in the first trimester of pregnancy, children under 15 Kg, and history of seizures. Mefloquine may cause dizziness, nightmares, psychosis and spatial judgment impairment (not recommended for pilots, drivers, scuba divers, mountain climbers). If mefloquine is contraindicated and Thailand is the destination, doxycycline 100 mg daily 1 to 2 days before and 4 weeks after leaving an endemic area, to deal with expected chloroquine resistance.

Proper use of window and door screens is paramount; clothes should cover most of the body. Travelers must use sleeping nets, insect sprays, and personal insect repellents containing 15% to 30% diethyltoluamide (DEET).

In the event of symptoms (high fever, headache, muscle, joint, stomach, and chest pain) the following advice is recommended: Seek immediate medical help. If medical help is not readily available, start self-treatment. In chloroquine-sensitive areas, this would consist of chloroquine phosphate 500 mg, then 250 mg 6 hours later, followed by daily chloroquine 250 mg. In chloroquine-resistant areas, mefloquine 750 mg is followed by 500 mg 6 hours later.

If mefloquine is contraindicated the physician locally (or upon return), should consider halofantrine (Halfan) or Pyrimethamine/sulfadoxine (Fansidar). In Thailand, due to the existence of multidrug-resistant *P. falciparum*, high-dose halofantrine is used, monitoring cardiac toxicity. Halofantrine contraindications are prolonged Q-T interval, pregnancy and breast feeding. Fansidar may rarely cause fatal cutaneous reaction.

Diarrhea

This is the main complaint of visitors to developing countries. Etiologies of travelers diarrhea are 80% bacterial (*E.coli*, shigella,

salmonella, and campylobacter), 10% viral, 10% parasites and others. Untreated diarrhea usually lasts for 5 days, and <24 hours if treated. The best prevention is caution in food and beverage ingestion. Prophylactic antibiotics are not recommended in general, but may be used in special circumstances.

There are three pretravel approach options: 1) no prevention; 2) bismuth subsalicylate (Pepto-Bismol) two tablets or one oz four times a day until 2 days out of the endemic area (maximum 3 weeks; will prevent 65% of diarrhea in the high-risk areas. Avoid when influenza or varicella virus are suspected due to danger of Reye's syndrome. Pepto-Bismol contains 262 mg bismuth subsalicylate per tablet or 524 mg per 30 cc; may blacken the tongue and stool); 3) antibiotics prevent 90% of diarrhea in the high-risk areas and are recommended for important short stays, presence of diabetes, and chronic diarrhea.

Antibiotic prophylaxis recommendations vary somewhat according to geographic area: For Mexico, nonCaribbean region: TMP/SMX (e.g., Bactrim DS) one every day until 2 days out of region; Mexico, Caribbean region, Latin America, Africa, South Asia: quinolones (norfloxacin 400 mg/d or ciprofloxacin 500 mg/d or ofloxacin 200 mg/d) until 2 days out of region.

Treatment

1. Oral hydration therapy.
2. Pepto-Bismol (liquid) 2 oz then 1 oz every 1/2 to 1 hour; max. 8 oz/24 hours.
3. Loperamide (Imodium) 4 mg then 2 mg after each loose stool; max. 16 mg/24 hours.

Contraindicated in bloody diarrhea.

4. Antibiotics: Ciprofloxacin 500 mg twice a day for 3 days, or 1 g every day for 1 to 2 days, or
ofloxacin 400 mg twice a day for 1 to 3 days, or
furazolidone (Furoxone) 100 mg four times a day for 1 to 3 days, or
Bactrim DS 2 tabs then 1 tab twice a day for 3 days.

Traveling Children

For all regions except Canada, Europe, Australia and New Zealand, typhoid vaccination is recommended. The oral vaccine may be used for age >2 years; parenteral for age 9 months to 2

years. For very high-risk areas the parenteral form is used for the 4- to 9-month age group.

Meningococcal meningitis immunization is indicated for age >2 years; Japanese encephalitis immunization for age >3 months. For malaria prophylaxis, chloroquine is generally well-tolerated; mefloquine may be used for children of weight >15 kg. Doxycycline may be prescribed for age >9 years. Halofantrine is approved for pediatric use, while fansidar is contraindicated for age <1 month. Breast feeding while on antimalaria medication is safe, except for halofantrine (1).

Antibiotic prophylaxis for diarrhea is not recommended for children. Imodium may be prescribed in diarrhea cases for age >2 years but should not take the place of diet control. Diarrhea may be treated with Bactrim combined with erythromycin. Generally, quinolones are acceptable for age >18 years. However, they may be considered for severe illness. One-half the adult Pepto-Bismol dosage is used for age >3 years, to be avoided when influenza or varicella virus are suspected.

Traveling During Pregnancy

Traveling is not contraindicated for normal pregnancies if to areas not distant from medical care. It is best done in the second trimester. Traveling more than 100 miles is not recommended during the third trimester due to increased risks of premature labor, preterm rupture of membranes, hypertension, phlebitis, and uterine and placenta injuries from motor vehicle accidents. A physician's permission is required by most airlines for domestic flights beyond 36 weeks gestation and 35 weeks for international flights.

There is higher risk for complications when there is a history of miscarriage, ectopic pregnancy, toxemia, preterm labor, incompetent cervix, prolonged labor, C-section, premature rupture of membranes, uterine and placental abnormalities, hypertension, and pelvic inflammatory disease. There should be pretravel discussion of signs and symptoms of obstetrical emergencies such as vaginal bleeding and fluid leak, lower abdominal pain, severe headache, blurred vision, ankle edema, increased BP, and decreased fetal movement.

Immunizations are relatively contraindicated in the first trimester, but may be offered when benefits outweigh the risks of side effects. Immunization for tetanus, oral polio, rabies, meningococcal meningitis, Japanese encephalitis, plague, yellow fever, and

hepatitis are the same as for general travel. Travel should be deferred for lack of immunity to measles and rubella. Typhoid fever vaccine, oral or parenteral, is to be given only for substantial risk, to be avoided in first trimester if possible. Cholera vaccine is to be used only in high risk and if required for travel to the region.

Malaria is more severe in pregnancy, carrying increased risk of abortion and preterm labor. Travel to areas of high malaria risk, especially including chloroquine resistant organisms, should be avoided. Chloroquine, however, is safe during pregnancy. Mefloquine may be used after the first trimester. Fansider may be considered as prophylaxis in extreme situations and for a single-dose treatment. Halofantrine is embriotoxic. Doxycycline is to be avoided in pregnancy, but usage may be required in chloroquine-resistant areas.

Near term Pepto-Bismol, quinolones, tetracycline, and Diamox are to be avoided, as are Hismanal and Seldane in the first trimester, as are iodine water purifying tablets for periods >2 to 3 weeks. Unpressurized high altitude is to be avoided due to increased risks of intrauterine growth retardation, HTN, and preterm labor.

For watery travelers diarrhea, Imodium may be used. Furozolidone is safe, as is Bactrim combined with erythromycin, except at term. Quinolones may be used for severe illness.

Medical Problems Attendant to Altitude

Partial pressure of oxygen (PO_2) at sea level is 21% of 760 mm mercury (Hg), 160 mm Hg. At an altitude of 18,000 ft, half the atmosphere is below (380 mm Hg) and $PO_2 = 79$. Alveolar PO_2 (PaO_2) is normally about 100 mm Hg, after subtracting the partial pressures of $PaCO_2$ and PaH_2O , the latter remaining constant at all ambient pressures, 47 mm Hg. Alveolar PO_2 falls with increasing altitudes, to 61 mm Hg at 10,000 ft and 46 at 15,000 ft. This is accompanied by falls in arterial blood oxygen saturation (ABOS) from 98% to 100% at sea level in a normal person to about 88% to 90% at 7500 ft and 33 % at 29,000 ft, the height of Mt. Everest. At 50,000 ft, the atmospheric pressure of 87 mm Hg is countered entirely by alveolar PCO_2 and H_2O , so that oxygen flow ceases, unless O_2 is delivered under pressure. Hypoxia attendant to decreased atmospheric pressures in the ranges encountered in mountain climbing and in nonpressurized flight is associated with short-term effects of increased pulmonary arter-

ial pressure and increased capillary permeability. Other problems of great altitude include the bends, due to emergence of nitrogen from solution in the form of bubbles, and their effects in various tissues.

Acute Mountain Sickness (AMS)

This is a constellation of symptoms that occurs increasingly as altitude rises above 8000 ft. Risk factors are younger age (<20 years), obesity, less than 1 to 2 days acclimatization time, fatigue, antihypertensive medications, current URI, moderate smoking, heavy drinking, and hypothermia. For the serious forms, high altitude pulmonary edema (HAPE) and high altitude cerebral edema (HACE), staying at altitude longer than 1 to 2 days is also a risk factor. Physical fitness is not necessarily protective and sex is not a factor. Table 48.4 gives the elevations of various common destinations in feet.

In 25% of people living near sea level milder symptoms occur at altitudes as low as 6500 ft, consisting of headache, poor performance, nausea, anorexia, dysphoria, peripheral edema, and light headedness; 50% will have these symptoms at 10,000 ft. Nearly all will recover by simply resting at altitude for 1 to 2 days and elevating the lower extremities for relief of edema. In the absence of other symptoms, many people will experience low stamina, unexpected sighing, and nocturnal Cheyne-Stokes breathing.

Both HAPE and HACE are medical emergencies. HAPE symptoms, usually occurring at 12,500 ft or higher, especially when ascent was rapid, consist of tachypnea, tachycardia, cough, frothy or blood tinged sputum, severe dyspnea, and weakness.

HACE symptoms and signs are increased drowsiness, unsteadiness, irritability, agitation, irrationality, hallucinations, and focal neurologic symptoms and signs.

Treatment of both HAPE and HACE consists of the following:

1. Descent as soon as possible.
2. Oxygen at 1 L/min for less severe symptoms, especially important during sleep when hyperventilation occurs normally; 4 to 6 L/min for severe symptoms.
3. "Simulated descent" in a one-person portable hyperbaric hand-pumped tent (Gamow bag, Portable Hyperbarics, P.O. Box 510, Illion, NY, 13357-0510, phone 315-895-7485). The therapeutic effects persist for only 1 hour after emergence

Table 48.4.
Elevations of representative destinations.

Destination	(State) County	Altitude	
		Feet	Meters
Addis Ababa	Ethiopia	8038	2450
Albuquerque	New Mexico, USA	4945	1507
Aspen	Colorado, USA	7773	2369
Butte	Montana, USA	6765	2062
Bogota	Colombia	8678	2645
Cheyenne	Wyoming, USA	6100	1859
Colorado Springs	Colorado, USA	6980	2128
Cuzco	Peru	11152	3399
Darjeeling	India	7431	2265
Denver	Colorado, USA	5280	1609
Flagstaff	Arizona, USA	6900	2103
Gallup	New Mexico, USA	6540	1993
Johannesburg	South Africa	5740	1750
Lhasa	Tibet	12002	3658
La Paz	Bolivia	11736	3577
Laramie	Wyoming, USA	7272	2217
Machu Picchu	Peru	8003	2440
Mexico City	Mexico	7347	2239
Mt. Everest (summit)	Nepal	29028	8848
(base camp)		16900	5150
Mt. Kilimanjaro	Kenya	19340	5895
Mont Blanc	Switzerland	15771	4807
Nairobi	Kenya	5450	1660
Pike's Peak	Colorado, USA	14000	4267
Quito	Ecuador	9249	2819
San'a	Yemen	7800	2377
Santa Fe	New Mexico, USA	6950	2118
South Pole Station	Antarctica	9186	2800
West Yellowstone	Montana, USA	6644	2025
Zermatt	Switzerland	5314	1620

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from the tent but the modality is useful when oxygen is not available.

4. Medications: acetazolamide, dexamthasone and nifedipine.

Acetazolamide 250 mg twice a day promotes hyperventilation through alkalinization of the urine and promotion of ventilation through induction of slight metabolic acidosis. Though it is accepted by all experts, it may stimulate ventilation beyond its production of acidosis, since acidosis has a detrimental effect on arterial blood oxygen saturation (ABOS) in the oxygen dissocia-

tion curve. A preventative dosage, started on the day of ascent and continued for 2 to 3 days, is 125 mg twice a day.

Dexamethasone 8 mg followed by 4 mg every 6 hours has been shown to decrease symptoms in high altitude situations, probably by reducing cerebral edema. It may be used in prevention, 4 mg every 6 hours starting on the day of ascent but, once started, must not be stopped abruptly due to the probability of precipitation (or exacerbation) of symptoms.

Nifedipine (Procardia, Adalat) 20 mg every 6 hours has the specific therapeutic action of reducing pulmonary arterial pressure. It has been used in the same dosage in the role of prevention, but its value in that regard has not been proved.

Prochlorperazine (Compazine) in ordinary antiemetic dosages increases ventilatory drive.

Prevention and Minimization of AMS

1. Spend at least a day at about 5000 ft before proceeding to ascend to altitudes above 10,000 ft.
2. Avoid strenuous activities for the first 1 to 2 days at altitude.
3. "Climb high but sleep low." Many cases of AMS begin at night.
4. Stay warm, dry and rested. Exhaustion predisposes to hypothermia, and both appear to increase chances of AMS.
5. Maintain adequate caloric intake (i.e., override mild anorexia); increase carbohydrate proportion to 70% (from an average of 50% to 60%), in order to generate more CO_2 and hence ventilatory drive.
6. Travel and climb in pairs and watch one another for signs.
7. Consciously breathe deeply (unproven).
8. Attend to risk factors in advance, whenever possible.
9. Follow pharmacological measures outlined above.

Air Travel

The most significant medical aspect of air travel is associated with the decreased atmospheric pressure attendant to altitude. Virtually all commercial air travel is done in pressurized jet aircraft, flying between 25,000 and 40,000 ft, or nonpressurized craft at levels below 10,000. The following are "cabin altitude" equivalents at corresponding ambient altitudes in pressurized commercial aircraft:

35,000 ft ambient	5000 ft cabin (comparable to Denver)
40,000 ft ambient	7500 ft cabin (nearly the altitude of Machu Picchu)

Since altitude sickness begins at altitudes above 8,000 to 10,000 ft, it probably does not exist caused by commercial air travel alone, unless flight is in unusual nonpressurized aircraft flying at altitudes up to 20,000 ft. In the latter cases, supplemental oxygen should be routinely supplied, which, at 20,000 ft should be delivered at 100%. It is possible that cabin altitude contributes to the jet lag syndrome, particularly fluid retention, which could occur on long flights at high cabin altitudes.

Air quality in commercial jet aircraft has recently been the subject of controversy. While earlier transports (DC-9, Boeing 727 and 747) provide 100% fresh air every 3 minutes, newer models (Boeing 757, 767 and A-320) provide 50% recirculated air and exchange it every 2 to 6 minutes. The latter standard exceeds government requirements for buildings on the ground, and the innovation saves the average airliner \$60,000/year (2).

Stable medical conditions are seldom contraindications to normal air travel. These include diabetes, stable angina, uncomplicated pregnancy, chronic renal failure, and controlled cardiac dysrhythmia. *Exceptions* are known pulmonary hypertension, otitis media (secretory or purulent), inability to clear the middle ears during symptoms of URI or allergic rhinitis (see Chapter 1), sinusitis or recent sinus surgery, noncommunicating lung cysts (blebs), thoracic surgery within 3 weeks, cyanosis, hemoglobin <8.5 gm/dL, sickle cell anemia.

Unstable contraindications to medical travel fall within two categories: 1) those that are symptomatic and generally in need of present medical care that is not available on civilian aircraft, and 2) those that are characterized by compromised oxygen and carbon monoxide exchange. In the former category is unstable ischemic heart disease; in the latter are hypercapnea ($\text{PaCO}_2 > 50$ mm Hg), hypoxemia ($\text{PaO}_2 < 50$ mm Hg) and diffusing capacity <50 percent of predicted. The remaining contraindications to air travel are two unstable conditions that involve pulmonary gas exchange: acute bronchospasm, dyspnea at rest, pneumonia, pneumothorax, and pneumopericardium.

Patients who have URI are at risk of painful barotitis, acute sterile secretory otitis media, sometimes with severe retraction of the eardrum and hemorrhage into the middle ear. This is one of the few problems of flight that can take place within a change of only a few thousand feet cabin pressure. It occurs upon descent, by virtue of the inability to repressurize the middle ears through eustachian tubes as atmospheric pressure increases in the cabin while

the middle ear pressure is at higher cabin altitudes (lower pressure). It does not occur upon ascent because expanding middle ear air more easily traverses the tube in the opposite direction. People should be advised not to travel by air unless they are able to “clear” the ears, i.e., force air into the middle ears by exhaling against the pinched nose with the glottis open (modified Valsalva maneuver). The accomplishment is both felt by the patient and seen by the examiner as tympanic membrane movement.

Jet Lag

A less serious aspect of air travel is “jet lag,” more likely on trans- and intercontinental trips. Most symptoms are the logical result of abrupt change in sleep patterns and resultant deprivation that produce dysphoria and contribute to fluid retention, also caused by physical inactivity and possibly cabin altitudes of 8000 ft for 6 to 8 hours. For some dehydration, due to low cabin humidity, may be an issue.

In rapid travel across time zone boundaries, travel from west to east involves time loss and potential difficulty in sleep onset while west to east travel, early fatigue and somnolence inappropriate to local time. Either change, combined with immobility, causes varying degrees of fluid “third spacing,” in proportion to the duration of the trip and size of time change per unit time traveled. Paradoxically, there may be mild hypovolemia. For blunting of jet lag symptoms, it would seem prudent to attenuate caffeine intake while traveling east across time zones and alcohol when traveling west. It is intuitive that one should maintain high water intake during flight and for several days after arrival, and obtain a good night’s sleep before the flight. Some feel one should avoid morning light and maximize evening light for the first few days after arrival at an eastern destination. Antijet lag diets have not proved to be effective.

Post-Travel Evaluation

An emerging concept is the routine health review of travelers after their return to the United States. It is suggested that it be scheduled before departure.

Asymptomatic Return

Basic evaluation for travelers for up to 3 months should be considered at 1 to 2 months after return, particularly in those who were sick or potentially exposed to tropical disease. This would

consist of a careful history and physical examination; CBC with eosinophilia, malaria smear and antibodies; stool culture for ova and parasites, and immunoassay for giardia; UA, HBsAg, RPR, HIV serology, malaria smear and antibodies, and schistosomiasis serology. Similar evaluation for long-term travelers (>3 to 6 months) is recommended as well, though it may be assumed that travelers who remain thus "indefinitely" are acculturated and have availed themselves of local knowledge, wisdom, and facilities.

Specific Symptoms, Evaluation, and Management

For returning travelers who are symptomatic (e.g., abdominal pain, diarrhea, fever, weight loss, fatigue, cough, and skin rash), a comprehensive evaluation is required. This consists of the same study as for asymptomatic individuals, expanded, depending on symptoms, to include blood chemistry, liver function tests, serology for hepatitis and STD; tuberculin skin testing, chest x-ray; serologic or skin tests for parasitic diseases and arbovirus; febrile agglutinins (brucella, tularemia, leptospira), Weil-Felix and/or indirect fluorescent antibody tests (Rocky Mountain and Mediterranean spotted fever, typhus, scrub typhus, and Q fever); sigmoidoscopy and rectal biopsy (schistosomiasis), spinal tap, CSF serology, CT or MRI scan (spinal cord schistosomiasis, neurocysticercosis), and ultrasound or CT of the liver (amebic liver abscess, hydatid cysts, toxocariasis, fascioliasis).

Fever. Attention should be directed to fever pattern and incubation periods. Life-threatening conditions such as falciparum malaria, typhoid fever, and Lassa fever are to be ruled out first. Physical examination may show a pulse slow for the level of fever, typical of typhoid fever. Typhoid fever may be diagnosed by culture of blood, urine, stool, bone marrow, and duodenum aspirate. West Africa Lassa fever may be diagnosed by blood culture, Lassa antigen, and immunofluorescent antibody detection. In addition to previously mentioned laboratory tests, a gallium study may be helpful for fever of unknown origin. When all is said and done, in most returning febrile travelers the cause is nonexotic, usually prostatitis or biliary tract disease.

Diarrhea. For acute diarrhea of less than 5 to 10 days, observe for ≤ 3 days while rehydrating orally, plus Pepto-Bismol except when influenza or varicella infection are suspected.

For chronic diarrhea of >10 to 14 days duration, previously mentioned stool studies are indicated, including fecal wbc and blood, stool culture, O + P $\times 3$, malaria smear (if patient is febrile and exposure were likely), *C. difficile* toxin (if prior antibiotic use). Empiric use of antibiotic may be considered.

Respiratory Symptoms. Most infections become apparent 6 months after exposure. One should have a low threshold for ordering chest x-ray (CXR), skin testing and CBC. Psittacosis is characterized by normal auscultation with infiltrate on CXR.

Hepatosplenomegaly. The differential diagnosis includes Q fever, psittacosis, leptospirosis, Rocky Mountain spotted fever (RMSF), malaria, toxocariasis, and echinococcus infection.

Rash and Skin Symptoms. Differential diagnosis includes helminthic infection, blastomycosis, paracoccidiomycosis, and RMSF.

Studies include culture and smears, scrapings with KOH preparation, biopsy for culture and histopathology evaluation. Serology should be obtained from lesions of returning travelers to establish diagnosis.

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Behavior and Psychology in Family Practice

Chapter 49

Counseling Models in Family Practice: Cognitive Strategies

Donald J. Tosi

This chapter highlights the cognitive therapies of Albert Ellis, Aaron Beck, and Maxie Maultsby, as well as our work in Cognitive Experiential Therapy. These models of counseling and psychotherapy have proved to be quite useful to practitioners and have gained widespread use in the field of psychology and behavioral medicine. The work of Ellis, Beck, and Maultsby will be summarized first, and a case demonstration of Ellis' Rational-Emotional Therapy will be presented. The system of Cognitive-Experiential Therapy, which makes use of hypnosis, will follow.

REASON, EMOTION, AND THE EXPANSION OF HUMAN AWARENESS

Rationality and the human effectiveness go hand in hand. Effective people generally operate to preserve their lives, maximize desirable emotions, achieve personal goals, strive to get along with others, and have a relatively good perspective on reality (1).

Human consciousness is dynamic, in that it shapes and is shaped by human activity as people orient themselves to life conditions. Consciousness is established through the process of socialization as it is encoded in language and semantics. Perception, for example, combines and translates what is sensed and perceived into a system of abstract and linguistic/semantic categories (2). Luria notes that in the course of a child's cognitive development a transition of thinking through new forms of mental dynamics appears. Logical reasoning, one aspect of mental dynamics, is fundamental to human cognitive activity.

RATIONAL AND COGNITIVE THERAPIES

Cognitive restructuring, fundamental to all cognitive therapies, is a mediating operation aimed at changing belief-disbelief systems (3). For example, a person's emotional response to a situation, therefore, is rarely due to the situation itself, but to the person's thoughts, beliefs, and attitudes about the situation. An event or stimulus (A) is perceived (B) in the context of beliefs and preconceptions regarding events such as A. Thus, A is assigned an effective evaluation, which results in an emotion (C). This may lead to a physiological response (D) and/or a behavioral action (E). Self-statements that reflect personal beliefs and disbeliefs influence people's emotions as well as motivate them to act in one way or another. When self-verbalizations are pessimistic, hopeless, or derogatory, they tend to produce anxious or depressed feelings (1). Table 49.1 outlines the permutations of the ABCDE model.

Ellis, the founder of Rational Emotive Therapy (RET), asserts that human irrationality is biologically rooted. Beginning with biologically determined needs for survival and self-protection, cultures have developed certain structures and rules for meeting these needs. Very early in life and continuing throughout the life span, human beings internalize useful cultural standards and rules that are often turned into absolutistic shoulds

Table 49.1.

The ABCDE model of interrelated elements of experience.

- A- Events (internal/external)
- B- Cognitive symbolic activity
 - b 1 Appraisal of events
 - b 2 Appraisal of response to events
 - b 3 Generalized appraisal of self/ego system
 - b 4 Cognitive/symbolic coping maneuvers
 - primary
 - secondary
- C- Affective responses
- D- Physiological/biochemical responses
- E- Behavioral responses

and musts. Because these beliefs are so ingrained; people are often not even fully aware that they hold them, let alone how they come about (3).

According to Ellis, when people become emotionally upset at point (C) about a situation (A), they have both rational beliefs (rB's) and irrational beliefs (iB's) about (A). Rational beliefs are expressed in the form of wishes, preferences, desires, and wants such as: *"I prefer to have others approve of things I do,"* or *"I don't like to have people disapprove of me for things that I don't do well."* These beliefs are more likely to lead to appropriate responses at (C), such as mild frustration, hope, sorrow, or regret. Irrational beliefs take the form of absolutistic demands characterized by shoulds, oughts, and musts: *"I must be loved by others,"* *"I must be perfect,"* *"I must be the best,"* and most likely lead to negative emotional states and inappropriate behavior (3).

A unique feature of Ellis' Rational Emotive Therapy is the use of E-prime language, eliminates the forms of the verb *to be* (i.e., is, am, was, were). In Ellis' cognitive restructuring scheme, the notion, *"I am a fallible human being,"* translates into *"I behave fallibly";* *"This is awful or catastrophic,"* translates into *"This situation causes me a lot of inconvenience."* Self-verbalizations such as *"I am worthless"* or *"I am wonderful"* reflect over-generalization that cannot be logically proved or demonstrated empirically. E-prime language, a more precise way of communicating with oneself and others, can help maximize self-affirming philosophies and minimize self-negating ones.

E-prime language can be a key mediator of left and right hemispheres of the brain and with direct implications for self-management strategies. For example, the idea that "*I am an idiot*," could be expressed as "*I acted idiotically*." The latter statement does not imply a rating of the whole self, only a behavior or an action. A more self-affirming and self-accepting philosophy can more easily be achieved through this kind of cognitive restructuring.

The following is a list of 10 irrational ideas and their rational counterparts postulated by Ellis (3):

Irrational Ideas

- * I must be loved and approved by others.
- * I must be perfect and achieving in all possible respects.
- * Many people are evil and wicked and they should be severely punished and reprimanded.
- * Life is horrible and catastrophic when it is not exactly the way I want it.
- * Events external to me cause me to become emotionally upset.
- * I should be overly preoccupied with fear and anxiety over future events that are potentially dangerous and uncertain.
- * It is easier to avoid life's difficulties than to face them.
- * I must have someone stronger than myself.

Rational Counterparts

- * I desire the approval of others for the things I do.
- * I desire to behave competently and achieve the things that are important to me.
- * Some people do act in stupid or bad ways and it is desirable to respond to them appropriately.
- * Certain life situations may not be the way I would like them to be, but that doesn't make all of life horrible and catastrophic.
- * I most probably cause most of my own emotional upsets by the manner in which I appraise those events.
- * Being concerned over potential dangers does not mean that I need to be overly preoccupied.
- * In the long run it is better to face one's responsibilities than to avoid them.
- * I am better off depending on my own resources.

- | | |
|--|---|
| <ul style="list-style-type: none"> * The past influences almost everything I do now or will do in the future. * I can achieve happiness by inertia, passivity, and inaction. | <ul style="list-style-type: none"> * My present behavior is largely due to the meanings I presently ascribe to the past and future. * Human happiness results from activity and involvement with people, places and things. |
|--|---|

Aaron Beck, rather than emphasizing irrational ideas as causes of emotional disturbance, postulates five systematic errors in thinking (4).

1. Arbitrary inference: drawing a specific conclusion in the absence of evidence to support the conclusions or when the evidence is contrary to the conclusion.
2. Selective abstraction: focusing on a detail taken out of context, ignoring other more salient features of the situation and conceptualizing the whole experience on the basis of the fragment.
3. Overgeneralization: the pattern of drawing a general rule or conclusion on the basis of one or more isolated incidents and applying the concept across the board to related and unrelated situations.
4. Magnification and minimization: errors in evaluating the significance or magnitude of an event that are so gross as to constitute a distortion.
5. Personalization: a proclivity to relate external events to oneself when there is no basis for making such a connection.

COUNSELING APPLICATION OF RATIONAL EMOTIVE THERAPY (RET)

This case illustrates the use of RET with a 40-year-old female executive with depressive symptoms. The therapist wastes little time educating the client about how irrational thoughts result in self-defeating emotions and behavior.

Rational Emotive Therapy

Darla, is president of a major east coast corporation. A routine physical examination was performed by her physician. She complained of a general feeling of malaise, low self-esteem, nervousness, fatigue, insomnia, and weight loss. No organic basis for her

symptoms were found, and her physician referred her to one of the psychologists in the group. Darla was referred to a woman counselor who specialized in executive stress.

Counselor: Hello, Darla, my name is Dr. Carla Jones. I understand Dr. Smith provided you with my name. How can I be of help?

Darla: Dr. Smith suggested that I have symptoms of mild depression. I'm not sure it's just not exhaustion.

Counselor: Your physical symptoms have been a source of irritation. Can you pinpoint a stressful event occurring in your life at the moment?

Darla: Not really . . . my life is going fine.

Counselor: How about work?

Darla: Well, my board is questioning my performance. Our stock has fallen from \$32.00 a share to \$21.00.

Counselor: Tell me more.

Darla: Well, the company's profits did not exceed last year's level.

Counselor: Did you become personally upset with the board's feedback?

Darla: Yes, I did. The economy has affected our company, and even so, the corporation is making money . . . but for some reason I am upset with myself. It's like I am not living up to their expectations.

Counselor: You mean you are telling yourself that, "If I don't meet some perfect standard of excellence, then I am a worthless person." As well, "the board" determines my worth as a human being.

Darla: Yes. For me to feel like a worthwhile person I must achieve the highest level of performance—the best. You know that as a woman you must far exceed normal expectations if you want the recognition, rewards, and success in the company.

Counselor: And if you fall short of perfectly achieving in all respects, you somehow seem less desirable to as a human being.

Darla: Well, that is how I feel.

Counselor: Do you think the philosophy that you must be the *best* executive, otherwise you're a personal failure, has something to do with the way you feel these days?

Darla: I never made that connection.

This is an example of how a person does not associate activating events (A), their beliefs about the event (B), and the resultant affective state (C). The counselor did not hesitate to focus Darla's attention on some of her perfectionistic and absolutistic demands, and how these might contribute to feelings of incompetence and symptoms of depression. Darla was quite quick to see those connections and gain a certain level of intellectual insight. Realistically, it may be some time before Darla internalizes more rational beliefs that would ultimately minimize her negative feelings. In the next segment, Darla inquires into the nature of depression.

Darla: If I am "depressed," just what is it, from your perspective?

Counselor: Depression often results when one negatively and dogmatically condemns oneself, and the world around them. Moreover, one usually takes a negative view of the future and believes oneself to be virtually helpless. For example, if the board judged your performance to be inadequate, and fired you, you might erroneously conclude that you were totally inadequate as a human being, as well as inadequate with respect to doing anything to rectify the situation. In effect, you might see yourself as a total failure. And that would be just awful. And in addition, you would most likely ignore many of your fine achievements, assets, and abilities.

Darla: That's a bit much, isn't it?

Counselor: Well, Darla, these notions may be worth consideration.

Darla: Look, I'm a very rational person most of the time. At times I think I might lose control—make a fool out of myself.

Counselor: Like there are two levels at which you are operating at the same time?

Darla: Yes. But that's illogical.

Counselor: Yes. Unfortunately human beings generally operate rationally and irrationally.

Darla: I was taught very early that I could not be irrational—that I must be perfect—otherwise I would never be a success.

Counselor: And a worthwhile human being?

Darla: Yes.

Counselor: Do you know any perfect humans?

Darla: No.

Counselor: Do you know many effective human beings—people who do certain things well?

Darla: Yes.

Counselor: Would you consider yourself a relatively effective human being?

Darla: Yes. I would.

Counselor: Could we reasonably assume you value personal effectiveness and will continually strive for it with a great measure of success?

Darla: Yes.

Counselor: Consider this question. What does perfectionism do for you?

Darla: Well, I believed striving for perfection was necessary for success.

Counselor: But you were striving toward *total* human perfection rather than excellence.

Darla: Maybe that's true . . . if you are perfect, no one will reject you. You won't have to worry about rejections anymore.

Counselor: I am not too sure about that. If, for the sake of argument, you arrive at a perfect state of being, you cannot be assured (1) that people will recognize it,

(2) that some people won't be jealous, and (3) that you won't worry constantly about maintaining that perfect state.

Darla: Well, that is a thought. I just never made those connections before. I never believed that emotions were connected to thinking. I thought emotions were automatic and the best way to deal with them was to ignore them.

Counselor: That works for a while, but rarely in the long run.

Darla: Yes. Well how long will it take for me to learn more about myself?

Counselor: I think six or eight sessions will help to provide you with some perspective.

The counselor engaged Darla in Socratic dialogue, yet zeroed in on the core elements of her problems. Over a period of several weeks the counselor assisted Darla's tendency to over-intellectualize her feelings. For homework, Darla was assigned *A New Guide to Rational Living* authored by doctors Ellis and Harper.

The counselor also took note of Darla's natural tendency to be perfectionistic, and in one of the later sessions the counselor made an issue of this point.

Darla: I liked the readings by Ellis—I think I found a new bible.

Counselor: I am glad you found the material interesting. However, it's not intended as a bible.

Darla: If I follow RET philosophy as an absolute, I should be super-rational.

Counselor: Ellis doesn't see reason as an absolute, or an end in itself, but as a means to accomplish certain personal goals in life.

Darla: Yes. I remember that point. But counselor, many of my symptoms have abated! I keep telling myself that "*I am probably of value to myself because I exist.*"

Darla, over the course of seven sessions, exhibited greater insight into the role of cognitive factors and their effect upon feelings and emotions.

Cognitive Experiential Therapy

Cognitive experiential therapy (CET) essentially assumes that cognitive processes whether they be conscious or unconscious be examined and can undergo significant modification. We found that hypnotic state appears to be a medium through which the cognitive modification of emotions and behavior can be more effectively accomplished. One aspect of CET differentiating it from other cognitive therapies is that it is stage directed. The stages are awareness, exploration, commitment, implementation, internalization/integration, and behavior stabilization. Another feature is that cognitive restructuring occurs along time (present, past, future) and awareness (conscious or unconscious) continua (5-9).

Hypnosis can enhance facilitation and figure into the expansion of awareness and rationality in human beings. Characteristics of hypnotic states include trance logic, suspension of critical judgment, and time distortion. In hypnosis or altered states of consciousness, responses to stimuli may be associated with either sympathetic or parasympathetic reactions and effects (10). Stimulus response cues can be selectively rearranged so they do not produce undesirable autonomic nervous system reactions.

Cognitive Experiential Therapy posits that a person's cognitions, emotions, and behaviors are best understood not only in the present time but past and future time as well. A person may be aware of some of these aspects but not others. The hypnotic state, given all its characteristics, assists in the interpretation of time (past, present, and future), and awareness (conscious/unconscious). Further, cognitive therapy is multidimensional, i.e., through a focused approach, it has tremendous implications for logical reasoning, and allows for the expansion of awareness and of creative imagination.

Emotions and the Self-System

Arnold defines an emotion as a felt tendency (sensation) to approach or avoid (behavior) a situation (internal/external event) judged or appraised to be suitable (cognitive appraisal) reinforced by specific bodily changes (physiological-biochemical), according to the type of emotion (11). Lazarus reinforces Arnold's early appraisal view of emotions and gives recognition to the role of unconscious processes and ego involvement in emotions (12).

The Cognitive Operations of the Self-System

The cognitive operations of the self-system are indeed complicated and varied (Table 49.1). Given the presence of external/internal events (A) that may activate cognitive and emotional responses, we have identified four related and simultaneously occurring cognitive symbolic operations (B): b1, b2, b3, and b4. B1 represents an appraisal, a belief, a judgment, and/or a meaning about the individual's response to the situation; i.e., thought, image, coping strategy, emotional-physiological response to the situation. B2 suggests a belief appraisal, judgment, and/or meaning about the individual's response to the situation; i.e., thought, image, coping strategy, emotional-physiological response, or behavioral response. B3 refers to a generalized appraisal, judgment, and/or meaning ascribed to the self-ego system. Generalized appraisal of the self-ego system, either positively or negatively, usually results in a intensification of a given emotional state.

B4 consists of primary and secondary cognitive-symbolic maneuvers that organize the self to respond to external and internal demands (coping). The primary maneuvers, largely instinctual, are utilized by the person to preserve and sustain life. The secondary maneuvers, generally learned, enhance or inhibit the expansion of awareness, personal growth, and development. Secondary maneuvers may be of a self-fragmenting or self-integrating nature. Examples of self-fragmenting maneuvers are repression, denial, projection, and irrational thinking. Self-integrating maneuvers are exemplified by creative thought and logical reasoning.

Both self-fragmenting and self-integrating strategies can *proliferate* given the way a person appraises at b1, b2, and b3. Proliferation is analogous to a chain reaction of all possible elements interacting with one another whether at a conscious or unconscious level. Proliferation is a dynamic force that motivates the person to act or to inhibit action.

Cognitive/symbolic coping maneuvers (b4) occur in both left and right hemispheres of the brain. Because a precise delineation is theoretical at best, it is safer to assume the equipotentiality of both hemispheres, with one hemisphere playing a more dominant role in one set of functions and the other with another set of functions.

The cognitive operations b1, b2, b3, and b4, are associated with and influence various emotional responses "C" (c1, c2, c3, c4 . . .). Rarely is a single emotion experienced when people

become upset. People usually respond with a range of emotions such as anxiety, hostility, guilt, and frustration that may vary in frequency, intensity, and duration.

Physiological and biochemical changes accompany emotional arousal. These, designated as "D" (d1, d2, d3, d4 . . .) also vary in frequency, intensity, and duration of occurrence. Typical physiological-biochemical responses are changes in heart rate, vasoconstriction/dilation, muscle tension/relaxation, and systolic and diastolic blood pressure.

Finally, at point "E," cognitive, affective, and physiological-biochemical responses translate into actions (e1, e2, e3, and e4). These actions, real or imagined, impact on the self and the environment and produce positive or negative consequences that increase or decrease the likelihood of a given behavior occurring in the future. These actions, too, vary in frequency, intensity, and duration. Behavioral consequences may be of a social nature occurring in the environment or may be self-administered.

AWARENESS AND TIME CONTINUA

A range of associations among cognitive, affective, physiological-biochemical, behavioral, and social experiences may be placed within the boundaries of awareness and time. Because one may not be fully aware how past events relate to present and future ones, an awareness continuum may range also from unconscious to conscious. Meaningful behavior in the present time usually is related to a remembered past and future expectations. This organization defines an experiential life space for a person.

When the self-system and all its elements operate so as to preserve the person's life, minimize stress, and facilitate the achievement of goals, the state of the organism is more functional and healthy. The converse is true when the self-system is characterized by incongruity, emotion and physical distress, and maladaptive behavior for prolonged periods of time.

Cognitive restructuring is a deliberate psychological strategy designed to challenge and neutralize self-defeating thoughts and feelings that emanate from interpersonal and intrapersonal conflict. Cognitive restructuring is more naturally a left hemispheric brain function (i.e., logical, critical, and evaluative thought). Subcortical structures of the brain and/or the right hemisphere, however, may not be influenced initially by such activity (1). Time distortion, tolerance of incongruity and inconsistency (trance logic),

and suspension of critical judgment are all aspects of hypnosis as well as right brain activity. Hypnotic states then may be utilized to help achieve some integration of both structures via cognitive restructuring. Hypnosis uses language and symbols most naturally processed by the right hemisphere of the brain to influence left brain functioning.

THE TECHNIQUE OF COGNITIVE EXPERIENTIAL THERAPY (CET) WITH PATIENT SUFFERING FROM ESSENTIAL HYPERTENSION

An abbreviated CET strategy for hypertensives is elucidated for the benefit of the clinician (9). The clinician should take note that CET is a relatively complex process that is directed through six stages: awareness, exploration, commitment, implementation, internalization, and stabilized behavior change.

It is assumed here that a thorough behavioral analysis of the psychobiology of hypertension has been conducted and that the patient is aware of the expanded ABCDE of human functioning (Table 49.2).

Therapist: Please close your eyes and begin to take slow, deep breaths. Establish a slow, rhythmic pattern to your breathing. Breathe slowly. Concentrate on your breathing so that with each rhythmic breath, you become very comfortable, and very, very relaxed.

Little or nothing interferes with your becoming very comfortably relaxed. (Slight pause.) (Use deepening techniques.)

Moreover, we are going to emphasize a clear, alert, and aware mind. And a mind that is free to concentrate and focus its attention on ideas and matters of personal significance to you.

I am going to count backwards from 25 to 0. Notice your ability to concentrate will be enhanced as you become deeply relaxed. Twenty-five, twenty-four, 23, 22, 21 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, 0. If you are comfortably relaxed, simply indicate by raising your left index finger. (Pause.)

In this state of relaxation, you can visualize very clearly many significant events in your life and are very capable of experiencing feelings about these past events in the present time, the past time, and the future time. Hypnosis is a state of expanded awareness, self-regulation, in that it can help free the mind to function in ways and assist one to manage one's own bodily responses and behaviors. Continue to relax and in time you can experience an almost complete absence of tension and complete freedom from

Table 49.2.
Multidimensional aspects of the psychobiology of essential hypertension: self-fragmenting and self-integration sequences.

(A) Events	
(Competitive relationship) Rejection by a significant person Denied recognition	
(B) Cognitive Symbolic Operations	
Self-Fragmenting	Self-Integrating
b1 I have been mistreated and can't stand it	I have been mistreated and can stand it
b2 I cannot concentrate	I can concentrate
b2 I feel rage and hate it	I feel rage; it's undesirable
b2 I hate not being able to express feelings	I dislike not being able to express my feelings
b2 I must be suspicious of people's motives	I can raise questions about people's motives
b3 I must be a winner at all costs	I desire to win
b3 I must not let anyone see me as weak	I can express weakness
b4 I am ready for anything	I can respond to situations
b4 I must be alert and on guard	I can be aware and alert
b4 I must suppress my rage	I can acknowledge my rage
b4 I must act impressively	I can act effectively
b4 I need to rely on someone	I can rely on myself
(C) Affective Responses	
Worry	Reduced worry
Frustration due to inhibited impulses toward overt action	Reduced frustration
Suppressed anger/hostility/resentment	Reduced anxiety/depression/guilt/hostility
Anxiety/depression/guilt/hostility	
(D) Physiological/Biochemical Responses	
Increased renin/catecholamines/sodium	Decreased renin/catecholamines
Increased systolic blood pressure -140 mm or more	Decreased systolic/diastolic pressure
Increased diastolic blood pressure -90 mm or more	Decreased pulse
Increased pulse rate	Relaxation
Excessive skeletal muscular tension	Increased energy
Fatigue	

Table 49.2 (continued).
Multidimensional aspects of the psychobiology of essential hypertension: self-fragmenting and self-integration sequences.

(E) Behavioral	
Conforms	Independent
Unassertiveness	Assertiveness
Yields in arguments	Takes a position

distraction. You can be as critical as you need be, yet you can suspend critical judgment temporarily if you desire.

Therapist: (Assume the person has achieved a mild to moderate hypnotic state.) Concentrate, if you will, on a few critical points about the ABCD's and E's of personal functioning we have previously discussed.

Reflect passively on some of those undesirable emotions that may have influenced your body's responses (i.e., increases in pulse rate and blood pressure), as well as how these undesirable emotions could influence inappropriate behaviors (i.e., a lack of assertiveness and other forms of self-inhibition).

Recall a disturbing event and allow your mind to reflect passively on the event. Remain as calm and as relaxed as possible. (Pause.) (Ask for Ideomotor Signal and client to verbally express what he/she is visualizing.) Perhaps you are experiencing feelings of threat and fear, or frustration and anger, feelings and emotions you normally tend to inhibit. (Pause.)

Notice as you hold back your anger or other feelings, you may observe various bodily symptoms (i.e., tension, fullness in the head, an increase in pulse), especially when you don't deal with the situation for fear of some reprisal. (Pause.)

Can you visualize that? (Ask for ideomotor response.) (Allow client to express himself herself and proceed slowly.) Perhaps you see yourself acting cowardly, unassertively, or inconsistently. You think others will disapprove of you, reject you, punish, or embarrass you. You may feel guilty—maybe frustrated—maybe enraged. (Pause.) Simply be aware of the feelings, as if you are observing at a distance. You may have noticed that at times you were unaware of these feelings and changes in your body. Now, observe how significant events we have labeled A have associated with your emotions labeled C, physiological

reactions labeled D, and behavioral tendencies labeled E. (Elaborate if necessary.)

Now, just take note of that sequence, visualize and continue to relax. (One minute or so of silence . . . and then proceed.)

Up to this time you have concentrated on A, C, D, and E in a negative sequence. Now, concentrate your attention on the thoughts, ideas, or beliefs you have about 1) the situation (b1), 2) your responses to the situation (b2), 3) yourself in that situation (b3). (Move slowly and ask client to share thoughts.)

If you don't mind, and for the moment, I can suggest some of the thoughts you reported earlier in this process. For the moment, just give consideration to them. You may simply express actual thoughts you are currently having if you would like.

Recall that when people experience disturbing emotional reactions such as rage, hostility, anxiety, and guilt, negative bodily reactions such as increased blood pressure may result and certain thoughts, whether conscious or not, can activate those reactions.

(Speak slowly.) Observe that your thoughts (B) are generally connected with A's, C's, D's, and E's. (Pause . . . Give examples.) (Take as much time as needed.) (Elaborate upon the ABCDE sequence.) Consider a situation in your life—a time in the present, past, or future where you believed a significant person such as your mother, father, friend, boss, teacher, husband, or wife placed you in a position where you felt intimidated. Can you do that? (Pause . . . Ask for Ideomotor Response.)

You may have been afraid that person would/could view you as a failure if you did not live up to their expectations and do something to hurt you—such as withdrawing their love and approval. Perhaps this person refused to give you the recognition you wanted and that you better be ready for something bad to happen. (Repeat, if necessary, very slowly.) At this time, simply reflect on this event, as you did earlier. (Pause.)

Now, concentrate on B—what you are telling *yourself about situation A*. For the time being, permit me to guide your thoughts or simply suggest some thoughts that you may be having. Is that acceptable? (Allow client to respond.) My suggestions are based on what we hypothesize about people's attitudes and thinking patterns associated with essential hypertension. Some of them may apply, then some may not. Of course, you are free to edit any of my suggestions in whatever ways you would like. Act as if you are detached from these thoughts.

I must be alert and on guard. (Pause.) (Repeat several times.) *I must be ready for anything.* (Pause.) (Repeat several times.)

I cannot let anybody get ahead of me—I must be an effective person and must not fail under any circumstances. I could not cope with failure. (Pause.) (Repeat several times.)

If I would fail, people would know that I am worthless or inadequate. (Pause.) (Repeat several times.)

I can't stand being placed in such a situation — I would like to strike out, but I had better inhibit my anger. (Pause.) (Repeat several times.)

I should never feel anger or express it. (Pause.) (Repeat several times.)

I must compete, but it frightens me because people, especially authorities, can somehow hurt me. (Pause.) (Repeat several times.)

I need some people to rely on, but this makes me feel so weak and inferior that I get very frustrated and angry, but can't seem to express it. I sometimes hate myself. (Pause.) (Repeat several times.)

I have found myself feeling this way in the past many times. I will always feel this way. (Pause.) (Repeat several times.)

Notice how thoughts such as “I must be alert and on guard,” frustrate you, produce anxiety, cause your blood pressure to rise, and lead to ineffective ways of coping or dealing with many life situations. (Pause and repeat.)

Visualize these thoughts, if you can. (Pause.)

Notice how you evaluate your situation (b1), your response to it (b2), how you evaluate yourself (b3), and how you select or use strategies that help you cope (b4). Each day you will become increasingly aware of how these ideas may influence your emotions, your bodily responses, and your behavior, and in time become increasingly accepting of these tendencies, less frustrated by them, and more desirous to overcome them. (Pause.) (Setting the stage for commitment.)

Momentarily, stop reflecting on these thoughts, feelings, bodily responses, and behaviors. Let yourself actually experience them somewhat. Notice you do feel anxious, frustrated and/or angry and can sense your blood pressure rising somewhat. You can even envision yourself acting ineffectively for the wrong reasons. (Pause.) (Repeat, if necessary.)

Now STOP. Relax and allow your mind to clear. (Pause for a minute or so and then proceed.)

Now we are going to move into a second part of this experience—a *cognitive restructuring* phase. This time you can visualize an alternative and a more self-enhancing ABCDE sequence—one that you have become aware of earlier.

Let's begin: (Speak slowly.) Imagine the same event(s) (A) in the previous sequence. (Pause.) Reflect on it for a moment. Visualize clearly the event. (Pause.)

This time, however, observe more self-enhancing thoughts at B. (Ask client to share thoughts.) Imagine something like this: "*I don't like what is happening to me or could happen to me in this situation. I can think clearly, respond to this situation calmly, and cope with it. If not, so what. I am hardly a failure as a human being.*" (Pause.) (Repeat, if necessary.)

I don't have to be overly preoccupied with this situation. How can anybody really disturb me—unless I allow them to? I can express myself and need not punish myself with blame, guilt, and fear. (Pause.) (Repeat, if necessary.)

I have the right to be frustrated at times and also have the right to express my feelings—even if people retaliate or disapprove of me. I don't have to personalize their behavior. (Pause.) (Repeat, if necessary.) (Allow client to elaborate and respond.)

Observe that these more self-enhancing thoughts and ideas can become associated with a lessening of tension—a lessening of anxiety—a lessening of anger. (Pause.) As you become calm, relaxed, and focused, your mind becomes clear. Notice how you can connect these more self-enhancing thoughts to more desirable feelings, bodily states, and behaviors. Further, imagine that your blood pressure decreases as your thoughts become more and more rational and appropriate. (Therapist reinforces the client's use of a self-enhancing cognitive strategy in real life situations.)

Notice as you translate more rational ways of thinking into more positive emotions that your blood pressure can become lower, and your behavior becomes more and more effective. In time, the lessening of tension, the lessening of anxiety, and the lessening of negative emotions such as anger become more natural.

Permit me to repeat and review the process of cognitive restructuring once again with the idea of internalizing these more constructive thoughts. The idea that "*I must be alert and on guard all the time, or else,*" simply translates into, "*I can be appropriately alert.*" The idea that "*I have to be ready for anything, or else,*" simply translates into "*If I am alert, I can be responsive.*" The idea that "*I cannot let anyone get ahead of me and cannot fail under any circum-*

stances," translates into, "*I can achieve a more effective life and can never be a failure as a human being.*" Notice that you are able to internalize more easily these thoughts.

I will now count from one to ten. When I reach ten, your eyes will open. One . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10.

CONCLUSION

The utilization of hypnosis along with cognitive restructuring has considerable merit in the management of psychological factors affecting physical conditions. The CET strategy has shown promise in the restructuring of person-environment interactions associated with a variety of psychosomatic illnesses (8).

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Depression

Kay A. Bauman

EPIDEMIOLOGY

At any given time in western nations, approximately 2% to 3% of men have a major depressive disorder and 5% to 9% of women. The lifetime risk for this disease is 7% to 12% for men and 20% to 25% for women. Most people with depression present between the ages of 18 and 44 years, with the highest incidence between 25 and 34 years, but this diagnosis is common in all ages, including the elderly (1, 2), and equally prevalent among races, incomes and education levels. Marital status affects men and women differently in that marriage decreases the risk of depression in men and increases depression in women, compared with their single counterparts. One particular occupation that has a high rate of depression and the potential consequence of suicide is physicians. Genetic factors are significant in depression: A history of depressive illness in a first-degree relative doubles the risk of depression compared with controls.

ETIOLOGY AND PATHOPHYSIOLOGY

Like many other diseases, depression has both genetic and environmental factors. Twin studies show that monozygotic twins reared together have a 75% concordance rate and 67% when reared apart. Dizygotic twins have only a 19% concordance rate (3). Nonetheless, for the presentation of an initial major depressive episode to occur, an environmental challenge such as a stressful life event or a psycho-social stressor is often required. This is much less likely to be the case with recurrent depressive episodes.

Original biochemical mechanisms studied in depression focused on the central nervous neurotransmitter systems, which included norepinephrine, serotonin, and dopamine. Recent research has focused on the role of the postsynaptic receptors as the site consistently altered in major depression. As more categories of antidepressants have come into clinical use and as each category becomes more focused in its biochemical action, we gain a clearer understanding of the specifics of the biochemical abnormalities in this disease.

There is also evidence of hormonal roles in depression. Both estrogen and progesterone have effects on the neurotransmitter systems and are linked to premenstrual mood changes, postpartum mood changes or depression, and perimenopausal mood disorders. Depression can also be associated with thyroid disease and corticosteroid abnormalities such as Cushing's disease.

DIAGNOSING DEPRESSION

The following table includes the DSM-IV criteria for a major depressive episode. Included are mood, activity, thought, sleep and weight changes, and social or occupational dysfunctions. Excluded considerations are a recent death in a family member, substance abuse, a general medical condition, and those who do not meet the criteria for a Mixed Episode (at least 1 week of rapidly alternating euphoria or mania with depression) (4).

Criteria for Major Depressive Episode

Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning: at least one of the symptoms is either 1) depressed mood, or 2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

- A. 1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by other (e.g., appears tearful). **Note:** In children and adolescents, can be irritable mood.
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others).

3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. **Note:** In children, consider failure to make expected weight gains.
 4. Insomnia or hypersomnia nearly every day.
 5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
 6. Fatigue or loss of energy nearly every day.
 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
 9. Recurrent thought of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
- B. The symptoms do not meet criteria for a Mixed Episode (see p. 335).
- C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).
- E. The symptoms are not better accounted for by bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

In a patient interview, the physician takes time to review the *family* history especially regarding depression, substance abuse and suicide, and the *personal* history for depression and suicide attempt, recent life events or stressors, sleep disturbances, weight changes, and general mood and energy levels. The high prevalence of depression suggests that the primary-care physician routinely include a few questions that will allow one to screen for depression. Positive responses, such as lack of energy, mood or sleep disturbance, or recent personal loss, call for a more thorough

assessment for depression. There are multiple depression screening tools available such as the Beck Depression Inventory, the Center for Epidemiological Studies-Depression Scale, and the Zung Self-Rating Depression Scale. There is also a section of the General Health Questionnaire on depression that is available for use in the ambulatory care setting. For women, specific questions regarding depression in the postpartum period, premenstrual syndrome, or perimenopausal mood changes may be appropriate. Once depression is being considered, the physician must recognize concurrent diagnoses that might be affecting the patient's presentation such as alcohol or substance abuse. A review of current medications will identify those that have long been associated with depressive mood changes such as some antihypertensives, corticosteroids including anabolic steroids, oral contraceptives, anticonvulsants, H-2 blockers, and others. However, consistent data documenting causative increased rates of depression exist for very few drugs, in particular reserpine, corticosteroids, and anabolic steroids.

TYPES OF DEPRESSION

There are multiple other mood disorders from which it must be differentiated. These include:

- Adjustment disorder with depressed mood, such as might be diagnosed in a recently bereaved patient.
- Dysthymic disorder, a chronic, i.e., at least 2 years, mood disturbance of lesser severity than major depression.
- Bipolar disorder: a cycling of major depression and manic episodes. Manic episodes include periods of persistently elevated mood and may include inflated self-esteem, decrease in need for sleep, pressured speech, rapidly racing thoughts, marked distractibility, increased agitation or activity, or excessive involvement in pleasurable activities without regard to their potential negative consequences (such as buying sprees, flings). Manic episodes also require that symptoms be severe enough to markedly impair the person's function or perhaps require hospitalization. Individuals with bipolar disorders have a high lifetime suicide risk, up to 19%.
- Cyclothymic disorder: like bipolar disorder, includes alternating cycles of mild depressive mood with abnormally elevated mood.
- Seasonal depression.

COMORBIDITIES

Depression and Alcoholism

Although the prevalence of alcoholism in patients with major depression is probably not higher than in the general population, many studies show that patients with alcoholism over time frequently suffer from depression. When the diagnoses coexist, alcoholism is generally the primary disease. Thus, treating the alcoholism often results in the disappearance of the depression. However, if the depression persists for greater than a month after withdrawal from alcohol, it is appropriate to treat the patient pharmacologically. Patients with these two diagnoses tend to have a poorer prognosis in resolution of the depression and have increased attempted and successful suicides.

Depression and Schizophrenia

This combination of diagnoses usually prompts a psychiatric referral. It occurs in approximately 25% of schizophrenic patients. Since depression accounts for approximately 50% of suicides and schizophrenia an additional 10%, these patients represent very high suicide risks. Because of the side effects of neuroleptics, the diagnosis of a coexistent depression is often difficult, and adjustments in medicines may need to be made to determine whether the depression is real or medication induced. In schizophrenic patients, antidepressant therapy works concurrently with antipsychotic medications. However, these patients often are seriously enough ill and present such a management challenge, they may ultimately need electroconvulsive therapy.

Depression and Anxiety Disorder

Concurrent anxiety symptoms are present in up to two-thirds of patients with depressive disorders (5). The reverse may be true, and the patient who first presents with a panic or other anxiety disorder may become depressed. Nonetheless, the presence of both anxiety symptoms and major depression results in a more severe disturbance and lower recovery rates than either alone and is a much greater challenge for management. The lifetime suicide attempt rate for this combined diagnosis is higher than with either diagnosis alone. The addition of the antianxiety drug buspirone to the antidepressant regimen is often useful.

Depression in Children

Although the prevalence of depressive disorders in children is estimated to be low, 0.15% to 2%, in a population of children with accompanying medical disease it is much higher, perhaps 10% to 20%. As in adults, females report significantly more problems with depression than males. Children who present with depression have a high risk of recurrent disease and more frequently have anxiety symptoms coexistent with depressive symptoms. Children with learning disabilities are at higher risk of depression. Depression is increased in adolescents compared with the prepubertal years. Since adolescence is a time of mood swings and increased emotionality, it can be difficult to determine who is at risk for major depression. Persistent depressed mood, poor functioning, particularly falling school grades and school absenteeism; or new or increased alcohol or drug use may point to a depressed teen. These youth need to be followed carefully for a potential manic episode (up to 20%) in the subsequent few years.

Depression in Geriatric Patients

The major burden of depressive disease in western countries is in young adults followed chronologically by lower incidences in the fifth and sixth decades. Thereafter rates steadily increase in the geriatric population such that after age 80, depression again becomes a common diagnosis. It is often overlooked in elderly patients because the mood disturbance is considered a normal part of aging. Elderly patients may have concurrent physical illnesses or be on one or several medications, which may contribute to depressive symptoms. Particular attention must be paid to the institutionalized elderly patient and the accompanying high risk of major depression. There is also an increasing rate of suicide in this population.

An important differential diagnosis to make in geriatric patients is between depression and dementia. The two may coexist, and if that is the case, treatment of the depression may result in improved function for the patient with dementia.

Depression in the Medically Ill Patient

As many as one-third of patients with chronic medical illnesses suffer from depressive symptoms. As a medical disease worsens, the rate of depression increases such that with hospital admission

at least 25% are depressed and with advanced cancer rates may surpass 50%. Depression must be considered a life-threatening complication of medical disease, and treatment of this secondary diagnosis will improve the patient's ability to cope with the problems of the primary illness. The diagnosis of depression in the severely ill patient presents a challenge because many of the neurovegetative symptoms used for the diagnosis of depression can be secondary to an illness such as Parkinson's or cancer. Risk of suicide increases significantly for many chronic diseases, e.g., by two to four times for cancer or chronic respiratory disease, 10 to 50 times for chronic renal disease with dialysis, 66 times for AIDS (6).

Depression and HIV Disease

As with the geriatric patient, depression with HIV/AIDS cannot be considered normal or understandable. The symptoms usually attributed to depression such as fatigue, decreased libido or sleep disturbance, can be symptomatic of HIV disease itself. For example, with depression, an HIV patient would *wake up* tired rather than tiring easily with mild exertion. A depressed patient has lost interest in previously enjoyed activities rather than not having the energy for them or conserving the energy for something more important (7).

Depression and the Changing Female Hormones

The postpartum period for a woman has risk for a depressive episode. Approximately 10% of new mothers will experience a major depressive episode in the first year after giving birth. Depression at this time is not qualitatively different than at a different time of life, yet the course can be shorter and somewhat milder. It is sometimes considered to be more like an adjustment disorder. Although menopause does not increase the rate of major depressive episodes in the general population of women, that time period is risky for recurrence of depression in women with a positive history. Depression is thought to be a side effect of oral contraceptives and may account for as high as 40% of the discontinuation of these drugs. Premenstrual syndrome is a mood disturbance that is limited to the luteal phase of the woman's cycle. The cyclic symptoms may match those of depression. An accurate diagnosis can be made if daily calendaring of mood changes is assessed.

MANAGEMENT

Although today we tend to manage major depressive episodes with antidepressive medications and/or psychotherapy, there is a natural course to this disease, that is one of spontaneous remission over 2 to 3 months. A postpartum depression may last a shorter period of time, and some untreated major depressive episodes may last longer, often 6 to 12 months.

Psychotherapy

Psychotherapy is an appropriate management, particularly for mild to moderate depression. Although response to psychotherapy alone may be slower than with pharmacologically management, therapy alone is highly effective, and for some groups of patients, is preferred. Psychotherapeutic efforts should be: 1) to increase the patient's coping skills, such as developing realistic approaches to minimize or solve a modifiable stressful situation, 2) to increase skills at managing the symptoms of depression, 3) to provide emotional and social support, 4) to readjust expectations about self or situation, and 5) to help patients identify and modify maladaptive ways of thinking about themselves or their problems. Adolescents, pregnant patients, and individuals with a situational depression are particularly likely to respond to psychotherapy. Family counseling or support groups may be of benefit, as well as environmental management such as avoiding certain situations, becoming active as a volunteer, or planning stimulating short activities. In general, an increase in pleasurable activities is helpful, as is exercise, if possible.

Pharmacotherapy

At the current time several major classes of drugs are used to manage major depression. Bipolar disease is managed with a different profile of drugs. In general, pharmacotherapy is highly successful in treating patients with a major depressive disorder such that approximately 60% to 80% of patients with moderate to severe depression will recover. There is little data to support the use of antidepressant medications with minor depression.

Since each category of antidepressant has a different mechanism of action, chemical structure, side effect profile, group of contraindications, therapeutic dose range, drug half-life, and cost, significant effort must be put into selecting appropriate therapy for the depressed patient. Generally the effectiveness of

an antidepressant should be assessed only after a 1- to 2-month trial period on the medication at a therapeutic dosage. Table 50.1 summarizes currently available antidepressants.

Major Classes of Antidepressants

Tricyclic Antidepressants (TCAs). TCAs are one of the oldest classes of antidepressants and the least expensive. They act by blocking the reuptake of norepinephrine and serotonin in the central nervous system. They may also act in part on other neurotransmitter systems such as those that utilize corticotropin releasing factor. The tertiary amine TCAs, amitriptyline and imipramine, are the most serotonin transporter selective of the TCAs. They have a severe side effect profile that can limit their usefulness. The secondary amines, nortriptyline and desipramine, are metabolites of the tertiary amines and have similar but milder side effect profiles. These major side effects are related to the inhibition of the wide range of neurotransmitter receptors. Blurred vision, urinary retention, constipation, dry mouth, and memory disturbances are related to the antagonism of the muscarinic/cholinergic receptors and the most common reason for discontinuing TCAs. Antagonism of the H-1 histaminic receptors is related to the hypertension, sedation, and drowsiness associated with TCAs. Serotonin receptor antagonism may contribute to the weight gain, hypotension, and sleep disturbances that can be seen with their use. Dopamine receptor blockade may cause extrapyramidal movement disorders and elevated prolactin levels. TCAs also have significant cardiotoxicity, which can result in conduction delays and arrhythmias. These cardiac effects plus the orthostatic hypotension and dizziness that can occur during TCA therapy may be related to the alpha 1 adrenal receptor antagonist properties of TCAs (8, 9).

The TCAs have a very low therapeutic index, the ratio between the median toxic dose and the median effective dose. Monitoring serum concentrations once at maximum dosage is appropriate. Since a several-day to 1-week supply of these drugs can be lethal when taken as an overdose, patients with a history of suicide attempts or ideation must be limited in the quantity of drug made. It makes sense for the primary-care physician to become well acquainted with one or two drugs from this category. Nortriptyline is often selected because of its less severe side effect profile and well-established therapeutic window.

In summary TCAs are effective antidepressants and relatively inexpensive, but their significant, broad side effect profile limits

Table 50.1.

Summary of the various categories of antidepressants, giving trade names, recommended starting and maintenance doses, advantages, prominent side effects, and approximate cost.

Category and Names	Trade Names	Recommended Dose Range (S-start) (M-maintenance)	Advantages/ Special Uses	Disadvantages/ Side Effects	Average Cost for 1 Month (at Average Dose)
TCAs			Generic forms often available; inexpensive, sedation can be useful side effect	Risk for fatal overdose; blurred vision, urinary retention, constipation, dry mouth; hypertension, sedation; weight gain, sleep disturbances; extrapyramidal movement disorders; cardiotoxic; conduction delays arrhythmias; hypotension, dizziness	
Amitriptyline	Elavil, Endep, generic	S-25 t.i.d. or 50–100 q.h.s M-75–300			S: \$9.50 M: \$9.50–18.00 S: \$9.00 M: \$9–12 S: \$67 M: \$67–132 S: \$27 M: \$27–46
Imipramine	Tofranil, generic	S-25 t.i.d. M-75–150			
Nortriptyline	Pamelor, generic	S-25 t.i.d. M-75–150			
Desipramine	Norpramin, generic	S-25 t.i.d. or 50–75 q.h.s. M-75–200			
Doxepin	Sinequan, generic	S-75 M-75–150	Less severe side effect profiles	Most severe side effect profiles	S: \$13 M: \$13–46

Table 50.1 (continued).

Summary of the various categories of antidepressants, giving trade names, recommended starting and maintenance doses, advantages, prominent side effects, and approximate cost.

Category and Names	Trade Names	Recommended Dose Range (S-start) (M-maintenance)	Advantages/ Special Uses	Disadvantages/ Side Effects	Average Cost for 1 Month (at Average Dose)
Protriptyline	Vivactil	S-5 mg t.i.d. M-10–15 t.i.d.	Once daily AM dosing, safe in overdose, not cardiotoxic	Nausea, headache, sexual dysfunction, dizziness, sweating, tremor; drug interactions with MAOIs, TCAs, some antiarrhythmics, some antipsychotics	S: \$69 M: \$94–139
Trimipramine	Surmontil	S-25 mg t.i.d. M-50 mg t.i.d.			S: \$75 M: \$150
Clomipramine	Anafranil	S-25 q.d. M-100–250 q.d.			S: \$33 M: \$130–260
SSRIs					
Fluoxetine	Prozac	S-20mg M-10–40mg	half-life of about 24 hrs; 2-week wash-out period half-life of about 24 hrs; 2 week wash-out period; plasma levels unaffected by age	Anxiety, insomnia, nervousness, anorexia; long half-life (2–4 days) and metabolites 7–15 days, thus very long wash-out period Dry mouth, somnolence Diarrhea	S: \$67 M: \$63–135
Paroxetine	Paxil	S-10–20 mg M-20–50 mg			S: \$40–75 M: \$75–300
Sertraline	Zoloft	M-50–200 mg S-50 q.d.			S: \$64 M: \$64–142

Table 50.1 (continued).

Summary of the various categories of antidepressants, giving trade names, recommended starting and maintenance doses, advantages, prominent side effects, and approximate cost.

Category and Names	Trade Names	Recommended Dose Range (S-start) (M-maintenance)	Advantages/ Special Uses	Disadvantages/ Side Effects	Average Cost for 1-Month (at Average Dose)
Fluvoxamine	Luvox		FDA approved only for obsessive compulsive disorder		
Venlafaxine	Effexor	S-25 t.i.d. M-75-300	Useful for refractory depression	Nausea can be severe, anorexia, insomnia, increased blood pressure and heart rate, increased serum cholesterol; multiple doses required	S: \$108 M: \$108-115
Heterocyclics					
Trazedone	Desyre, generic	S-50-100 mg q.h.s.	Minimal cardiotoxicity, minimally anticholinergic, few drug interactions except with MAOIs	Priapism, orthostatic hypotension	S: \$12-17 M: \$30-82
Nefazodone	Serzone	M-200-600 mg S-100 mg b.i.d. M-300-500 mg	No orthostatic hypotension, sexual dysfunction or sleep impairment	Twice daily dosing required	S: \$57 M: \$85-138
Bupropion	Wellbutrin	S-100 mg b.i.d. M-300 m	Helpful for coexistent anxiety; minimal cardiotoxicity, safe in	Seizures, insomnia, agitation	S: \$57 M: \$85

Table 50.1 (continued).

Summary of the various categories of antidepressants, giving trade names, recommended starting and maintenance doses, advantages, prominent side effects, and approximate cost.

Category and Names	Trade Names	Recommended Dose Range (S-start) (M-maintenance)	Advantages/ Special Uses	Disadvantages/ Side Effects	Average Cost for 1-Month (at Average Dose)
Amoxapine	Asendin	S-50 t.i.d. M-100 t.i.d. (or 300 q.h.s.)	overdose, few drug interactions except with MAOIs Both antidepressant and antipsychotic effects	Blurred vision, extrapyramidal effects	S: \$128 M: \$229
Maprotiline	Ludiomil	S-75 mg M-75 mg b.i.d.	Anxiety-associated depression	Nervousness	S: \$35 M: \$70
MAOIs					
Phenelzine	Nardil	S-15 mg t.i.d. M-20–30 mg t.i.d. (can be reduced after response)	Refractory depression, atypical depression, bulimia, panic disorder, concomitant anxiety, and depression; no anticholinergic effects	Cross react with tyramine containing foods (e.g., cheese), multiple common drugs such as decongestants, meperidine, TCAs, SSRI, and other antidepressants; dizziness orthostatic hypotension, weight gain, sexual dysfunction	S: \$47 M: \$47–92
Tranylcypromine	Parnate	S-10 mg t.i.d. M-30–60 mg t.i.d.			S: \$55 M: \$55–180

their use as first-line therapy. They are highly toxic when taken in overdose. Thus TCAs have become a second- or third-line medication for major depression (8).

Selective Serotonin Reuptake Inhibitors (SSRIs). SSRIs have rapidly become the most prescribed category of antidepressants in the United States. The drugs are highly selective for serotonin transporter inhibition and have comparatively weak interaction with the nonserotonin neurotransmitter receptors. The potent selective inhibition of serotonin reuptake at the presynaptic terminal results in an increase in serotonin availability. Since the SSRIs have little effect on the norepinephrine and dopamine transporters and a low affinity for the histamine, muscarinic/cholinergic, and alpha adrenergic receptors, their side effect profile is considerably less toxic to the individual patient. Major side effects are nausea, headache, dry mouth, insomnia, nervousness/agitation, sweating, dizziness, and tremors, most of which are transient. A significant problem can be sexual dysfunction, which is manifested as ejaculatory delay and impotence in men and anorgasmia in women. This side effect may require reducing the dose of the SSRI or switching therapy to another class of antidepressant.

There are also specific side effects for specific SSRIs. Sertraline is frequently associated with diarrhea, fluoxetine with anxiety, nervousness and insomnia, and paroxetine with dry mouth and sleepiness. However, the important cardiotoxic effects of the TCAs are generally not found with the SSRIs. There is a much smaller therapeutic dose range for the SSRIs and in many patients, the physician can begin therapy with a full therapeutic dose. In the elderly, lower doses are appropriate. SSRIs are also safer in overdose situations. As with the TCAs, there is a 3- to 5-week lag before the clinician can see a full therapeutic effect; thus one should wait a full 6 to 8 weeks before considering a change in therapy.

A major difference among the available SSRIs is their half-lives. For example, fluoxetine has a half-life of approximately 2 to 4 days, and its active metabolite of norfluoxetine has a half-life of 7 to 15 days. Thus, it takes several weeks to achieve a steady state concentration with fluoxetine, and in the same way, 5 weeks to achieve wash-out of drug and active metabolite. The half-life of sertraline and its active metabolite is considerably shorter than that of fluoxetine. It can reach steady state plasma concentra-

tions within a week. Paroxetine has no active metabolites and has a mean half-life of approximately 24 hours, so that steady state plasma concentrations can be reached in approximately one week. Because sertraline and paroxetine have shorter half-lives and also cause less anxiety, nervousness and insomnia than does fluoxetine, they may be preferred for patient management. However, the longer half-life of fluoxetine gives better protection from breakthrough of symptoms if a dose is missed, and withdrawal symptoms are less likely if it is discontinued. Because all SSRIs are metabolized extensively in the liver by the cytochrome P450 microsome enzyme system and are potent inhibitors of the IID6 isoenzyme, this results in significant drug-drug interactions. Higher plasma concentrations of antiarrhythmics, TCAs, some benzodiazepines, codeine, and others may result. Since sertraline has significant less effect on P450 enzymes, it is safer in this regard (10). SSRIs are costlier than TCAs. For example, a month's supply of sertraline is about \$60 compared with about \$8 to \$10 for a generic TCA. However, recent studies of patients treated with SSRIs show fewer lost work days and reduced dropout rates. Factoring in these economic benefits, the total cost of treatment was approximately \$300 to \$600 less with SSRIs.

Venlafaxine. Venlafaxine, an oral antidepressant marketed in 1994, is unrelated to either the TCAs or the SSRIs. Like the TCAs, it inhibits *both* serotonin and epinephrine reuptake. It does not, however, affect cholinergic, histaminic, and adrenergic receptors. Venlafaxine is rapidly absorbed and reaches peak plasma concentrations in 1 hour and steady state concentrations in 3 days. Doses of venlafaxine range from 75 to 300 mg/day in 2 to 3 divided doses. It seems to have less drug interactions than other antidepressants. Like the SSRIs, venlafaxine is metabolized primarily in the liver. Thus with both hepatic and renal impairment dosage needs to be decreased. The pharmacokinetics do not seem to be affected by patient age or sex.

Side effects resemble those of SSRIs, and patients usually develop a tolerance to the nausea and somnolence. There are still not adequate data on sexual dysfunction. Venlafaxine therapy may increase blood pressure and heart rate. This drug also is safer in overdose than TCAs.

The particular patient who might benefit from venlafaxine is the severely depressed, melancholic patient, or the treatment-resistant patient (11).

Heterocyclics.

Triazolopyridines. Trazodone and nefazodone inhibit serotonin reuptake and antagonize 5 HT₂ receptors; they are metabolized in the liver by the cytochrome 450 system. Trazodone is the oldest drug in this category and was marketed as an alternative to TCAs. By comparison, it had little activity at cholinergic, histaminic, dopaminergic, and adrenergic receptors, was far safer in overdose, and had few known drug-drug interactions. It is very sedating, a side effect that can be useful in the patient with severe insomnia. However, it is a relatively weak antidepressant and is often used as an "add on" drug in low doses for its sedating effect or for patients resistant to SSRIs. Orthostatic hypotension can occur in elderly patients and can limit its use. In some cases trazodone has caused priapism. Effective dosage ranges are 200 to 600 mg, but the sedation requires beginning with a 50 to 100 mg dose at bedtime.

Nefazodone is an effective and well-tolerated antidepressant recently available in the United States. It has a better side effect profile than trazodone. It does not cause orthostatic hypotension, priapism, sexual dysfunction, or disruption of sleep patterns. Like trazodone, it is sedating, though less so, and requires multiple daily dosing. It is rapidly absorbed and reaches peak plasma concentrations in an hour (11) and steady state in 4 to 5 days. In elderly patients, a given dose reaches a higher plasma level and is eliminated more slowly. Dosage ranges are from 300 to 600 mg/day, half of that for the elderly. Drug-drug interactions can occur with terfenadine and astemizole, alprazolam and triazolam, calcium channel blockers, and others (11).

Aminoketones: Bupropion. Bupropion is as effective as the TCAs and SSRIs and has few of the adverse side effects of those categories. It blocks dopamine reuptake and has minimal effects on serotonin or norepinephrine receptors. It has no cardiovascular toxicities, does not cause sedation or cognitive impairment, is relatively safe in overdose, and has no significant problems with drug-drug interactions.

Disadvantages for bupropion, however, are its requirement for multiple daily doses, for example 150 mg twice daily, a narrow therapeutic index, an increased risk of seizures, and it causes agitation and insomnia in a significant number of patients.

Monoamine Oxidase Inhibitors (MAOIs). This category of antidepressants was the first discovered. Isoniazid is an MAOI and

was noted to elevate the mood of depressed patients in TB sanatoriums. MAOIs block monoamines, e.g., norepinephrine, serotonin, and dopamine, in synaptic terminals and thus increase effective concentrations of these drugs. They have no muscarinic-cholinergic effect. At the present time, MAOIs are not considered first-line antidepressants. Significant cardiovascular and other side effects such as orthostatic hypotension can cause falls in the elderly. Severe cross-reactivity with tyramine rich foods (e.g., cheese) or several common medications such as the decongestants phenylpropanolamine and pseudophedrine in over-the-counter cold preparations can cause hypertensive crises resulting in strokes and fatalities. Hyperpyrexia can occur when meperidine and MAOIs are taken together (12).

Another danger with MAOIs is their interaction with other antidepressants such as high dosages of TCAs, combined with which they cause hyperpyrexia. They also interact with the SSRIs by causing a serotonin crisis called serotonergic syndrome. Patients will have tachycardia, hyperactivity, hypertension, and can progress to cardiovascular collapse. Fluoxetine has such an extended wash-out time, MAOIs must be avoided for up to 5 weeks after it is discontinued. Wash-out periods of 2 weeks are required for the shorter acting sertraline and paroxetine.

In spite of these side effects, MAOIs do have a place in the treatment of depression but more likely for refractory and atypical depressions. Like other antidepressants, a trial of 4 to 6 weeks is required for significant improvement to be observed (8).

GENERAL MANAGEMENT

Once a course of action is undertaken, the clinician can expect that 65% to 80% of patients will respond to treatment. Frequency of visits can be determined by considering whether the primary-care physician is also acting as therapist or counselor, the severity of depression and suicidality if present, the timing of the encounter related to the time line of the disease, and the need for monitoring of drug side effects, treatment compliance, or to monitor increasing drug doses. Unfortunately, frequency of visits may be affected by insurance reimbursements. Close follow-up, usually every 1 to 2 weeks, is indicated for at least the first 1 to 2 months.

If no response occurs by 6 weeks at a therapeutic dosage, a different antidepressant, often from a different category, should

be tried. Duration of treatment for the first major depression should continue for 6 to 9 months after response. Recurrent episodes require longer treatment at full dose, perhaps for several years or may be lifelong.

Patient education about the disease of depression, including the course of the disease, is extremely important. Office brochures, self-help books, or pamphlets can be helpful. Alternative or additional therapies can be exercise, religious counseling, social tasks, journaling or many others.

Referral to a psychiatrist should be considered for a depressed child, refractory depression, a suicidal or homicidal patient, psychosis, severe anxiety or agitation, manifestations of a bipolar disorder, and recurrent or relapsing illness. These conditions may require hospitalization. Other comorbidities that can suggest psychiatric referral are drug or alcohol abuse, panic disorder, or chronic pain syndrome.

COMPLICATIONS

Suicide

Individuals with major depression are at high risk for suicide. Suicide is the second most preventable cause of death (after lung cancer), the eighth leading cause of death in the United States and the third leading cause of death for 15- to 19-year-olds. Mortality has increased in white urban adolescents and adults in North America and Europe in the last three decades.

Although depression and suicide attempts are more common in females, death rates are higher for males. Questioning a patient regarding suicidal thoughts and/or plans does not "put an idea into one's head" or increase the rate of suicide. A history of a previous attempt, a family history of suicide, and specific plans and means are all risks for a suicide attempt, and hospitalization should be considered. Patients who don't respond to antidepressants (approximately 20%) or only partially respond and continue with significant symptoms have an increased risk of suicide.

Major drugs used for overdose are, in order, alcohol-drug combination, heroin overdose and TCAs. In teenagers, the method most used in suicide is overdose with TCAs. Approximately three-quarters of patients who overdose on TCAs do not reach the emergency room alive (10). Of help in assessing a suicide attempt is extent of premeditation and the likelihood of res-

cue. Leaving a note suggests seriousness! Any attempt must be regarded as serious, however, since most successful suicides occur in people who have made earlier attempts or gestures. In teenagers, a suicide attempt may be a desperate try for conflict resolution. Short-term hospitalization is usually in order, and provides the opportunity for psycho-social assessment, psychiatric referral and follow-up, and individual and family therapy.

Recurrent Illness

Patients who are refractory to antidepressants and in whom severe symptoms persist for many months, also have an increased relapse rate once they do improve. Long-term pharmacotherapy can be preventive for recurrent depression.

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Anxiety, Phobias, and the Undifferentiated Primary Care Syndrome

Gerald F. Ronning

Anxiety, depression, mixed anxiety/depression and somatization are the most common mental symptoms seen in primary-care medicine (1–5). Almost half of the patients you will see will have some combination of these symptoms, and you will spend almost half of your time in the assessment and treatment of these problems (2). You will refer very few of these patients, and treat 15 or 20 times more patients with psycho-social problems than you will refer to your mental health colleagues (6). You will use a combination of verbal therapy and/or tranquilizing and anti-depressant medications. By far most of your patients will do well and recover within a year.

The primary-care physician has been the subject of a great deal of attention and criticism over the years for supposed deficiencies in the identification and treatment of mental disorders. The primary-care physician has been courted, exhorted, treated, preached to, studied, measured, tested, taught and written about, all to no apparent avail, according to the current literature on the subject.

While this may be interpreted as a reflection of stubbornness or intractability (or worse) on the part of the primary-care physi-

cian, I think that a more likely answer is that the procedures and categories of the mental health specialties aren't always relevant to the realities of the primary-care setting. In primary care especially, the whole is always more than the sum of its parts, and the patient is more than the sum of the diagnoses of precision that might be applied. The primary-care patient cannot be reduced to or defined by the criteria and models of the mental health disciplines. And this is what constitutes, from the mental health perspective, underdiagnosis. It is therefore assumed that large numbers of patients with "hidden" psychiatric disorders are being harbored by the primary-care physician (7) in a "de facto" (read "inferior") mental health system (8). However, according to Jenks (9) "hidden psychiatric morbidity" in primary care may be less problematic than originally thought, in that studies tend to show that such morbidity can be accurately recognized and identified by the primary physician, even if it is rarely recorded in charts (i.e., in terms of the mental health system's syndromal categories).

In the primary-care setting, it seems clear that more stringent and rigorous diagnostic screening efforts to ferret out "hidden" mental disorders may represent an intrusion that is potentially disruptive of the doctor-patient relationship and unsuited to the effective treatment of the patient. While a significant number of patients will meet DSM-IV criteria for a mental disorder, most are a mixed combination of anxiety, depression and somatization that are "subsyndromal," from the perspective of psychiatry and probably unique to primary care (10, 11).

The notion that the doctor is missing a large number of mental disorders and inappropriately or inadequately treating those that are identified is based on a fallacy that diagnostic classifications that have been elaborated in the mental health setting can be directly applied to the undifferentiated patient seen by the primary-care physician (12).

The patient in the primary-care setting of family practice is not the same patient who is seen in other settings. I have often been humbled at how difficult it is to make mental disorder diagnoses of precision in the course of precepting residents in the family practice clinic. This experience has also been documented in an article describing a study in which the primary-care physician who, with identical psychiatric training as his psychiatric colleague and coauthor, disagreed in 30% of the cases that the psychiatrist identified as psychiatrically disturbed (6).

In addition to covering anxiety and the phobias, this chapter is intended to identify and characterize the essential and unique ways in which mental disorders are manifested in the primary-care setting and how and when a more precise syndromal characterization of the “undifferentiated primary care syndrome” as a specific disorder might serve to guide treatment and management. Once identified, the techniques and procedures that are familiar to the doctor will be effective in treating most of the mental disorders commonly seen in the clinic (13).

Anxiety in Context: The DSM-IV PC and the Undifferentiated Primary Care Syndrome

The Diagnostic and Statistical Manual of Mental Disorders, Primary Care diagnoses are summarized in Table 51.1. It is the result of a multidisciplinary collaboration in response to the putative under-recognition of mental disorders in primary-care settings (14). It is derived from DSM-IV, the standard diagnostic reference among mental health professionals, which has not been widely used by primary-care physicians. The Primary Care version is intended to be less complicated and to focus on con-

Table 51.1.
Classification of mental disorders in primary-care settings from DSM-IV PC.

Anxiety disorder due to:	
General medical condition	293.89
Alcohol	291.8
Substance, other, including medications or (Anxiety may be due to other mental disorders)	292.89
Panic disorder with agoraphobia	300.21
Panic disorder without agoraphobia	300.01
Phobias:	
Social	300.23
Specific	300.29
Separation anxiety disorder	309.21
Obsessive-compulsive disorder	300.3
Post-traumatic stress disorder	309.81
Acute stress disorder (symptoms last less than 4 weeks)	308.3
Generalized anxiety disorder	300.02
Adjustment disorder with anxiety	309.24
Adjustment disorder with mixed mood	309.28
Anxiety disorder not otherwise specified	300.00

ditions commonly seen in primary-care settings. It is epidemiologically organized to reflect the most common disorders first.

Even with the changes in the Primary Care version, however, this classification still does not lend itself well to the real experience in the clinical situation. As we will see, certain common clinical presentations, which may be unique to primary care, don't yet achieve the status of a disorder in terms of DSM-IV.

The overlap between anxiety and depression is considerable, and it has been proposed that a specific DSM diagnosis of mixed anxiety/depression be established to accommodate this common clinical presentation in primary care settings. This classification now does appear in the ICD 10 (2, 10).

Anxiety also frequently accompanies or precedes medical illness and, when associated with depression, it may become further obscured. Somatization of emotional distress is a common phenomenon in primary care (30% to 75% of physical symptoms lack an organic cause), and these mixed clinical presentations may account for a significant proportion of so-called hidden psychiatric morbidity (1, 4, 5).

The elaboration of a specific primary-care syndrome therefore seems justified.

In order to make classification more consistent with experience and to exploit the advantages of DSM-IV, I suggest that we merely turn the whole thing upside down and place the bottom, residual categories of the most common disorders (anxiety, depression, and somatization) at the top and give it a name: Undifferentiated Primary Care Affective Syndrome. The primary-care syndrome sits astride or transcends several DSM-IV categories. In this way, we can correlate algorithms of classification and treatment in a consistent manner that both respects the doctor-patient relationship unique to primary care, and supports the psychosomatic unity of the undifferentiated primary-care patient.

Making the Diagnosis

When anxiety symptoms are most obvious, for example, with acute panic attack, the diagnosis is not difficult, once medical causes have been eliminated. However, the typical patient with anxiety tends to avoid seeking medical attention and often does not mention anxiety symptoms to the doctor. The patient is often ashamed of his/her symptoms, attributing them to some moral weakness. They are concerned lest they be seen to be "running to the doctor all the time."

Unfortunately, the patient in the clinic often presents with

symptoms that are intermixed with acute or chronic medical problems, with a variety of somatic complaints that are not fully explained by a medical condition, or with depression (1). It is well-known that anxiety and depression coexist in most cases and that the differentiation between the two is a statistical accomplishment rather than a clinical reality. It is also well-established that mixed syndromes are far more disabling and associated with higher rates of suicide.

When masked by character structure or by a physical presentation, the diagnosis is often made by exclusion, frequently a futile and endless process. Furthermore, individuals with recent anxiety disorders have a greater prevalence of medical disorders, and there is a greater prevalence of multiple chronic medical conditions in patients with diagnosed psychiatric disorders (12, 14).

In assessing the patient, it is important to maintain an attitude of “evenly hovering attention” with tolerance for the imprecise and the ambiguous, which characterizes the undifferentiated syndromes. This ensures the creative balance between diagnoses of precision and diagnoses of depth required in primary care. Further, it evades premature closure, allowing for the emergence of underlying anxiety or depression through support of the doctor-patient relationship.

DIFFERENTIATION: PHOBIAS, PANIC, AND CHRONIC ANXIETY

Doctors often treat effectively without a precise diagnosis. However, failure to respond to nonspecific measures is an indication for reassessment and a different treatment approach. In many cases, a more precise diagnosis of the symptoms will permit more accurate, specific, targeted treatments and better prognosis.

General Features of Anxiety Disorders

Pathological anxiety is an extremely distressing and disabling symptom that is associated with intense autonomic arousal, primarily sympathetic, a wide variety of unpleasant physical symptoms, along with a sense of dread or foreboding. Unlike normal or signal anxiety, it is out of proportion to any real threat and interferes with adaptive efforts at mastery, leading to flight, phobic avoidance, or obsessional thinking and rituals.

Anxiety disorders can be differentiated on the basis of a number of criteria that then constitute distinctive groups with significant differences in their onset, course, psychopharmacology,

symptoms, genetic, demographic characteristics, response to medical and psychological treatments.

The DSM-IV classification arranges the anxiety disorders according to a hierarchy that places the most specific and inclusive conditions high on the list, beginning with medical conditions, and descending to the nonspecific categories, which tend to merge with the character disorders and neurosis, as well as other DSM-IV disorders, especially panic and phobia.

This hierarchy tends to parallel in a rough sort of way, the kinds of treatment modalities that will be effective, from the more specific, targeted medical model at the top to the more general, and nonspecific measures at the bottom. Panic disorder, which is at the top of the hierarchy, is the most likely to be found as a sole diagnosis, while generalized anxiety disorder is almost always present along with other disorders, such as depression, other anxiety disorders, or substance-related disorders (15).

Physical Signs and Symptoms of Anxiety

Sweating	Numbness and tingling
Lightheadedness	Air hunger, hyperventilation
Syncope	Tremor
Diarrhea	Urinary frequency
Dry mouth	Flushing
Tachycardia	Vomiting
Palpitations	Tetany
Sighing	Anxious demeanor—restlessness
Tachycardia forceful heartbeat	Butterflies
Dizziness	Sexual dysfunction
Nausea	Pallor

Differential Diagnosis

Medical conditions:

Hyper-hypothyroidism
Hypoglycemia

Cardiovascular conditions
Neurological conditions,
 seizures

Respiratory conditions:

Toxic and deficiency states
Other endocrine disease

Infection
Ménière's disease
CNS conditions

Psychiatric conditions:	
Other anxiety subtypes and panic states	Intoxication
Alcohol withdrawal	Somatoform disorders
Mania	Dementia
Depression (especially agitated)	Drug abuse/drug withdrawal
Schizophrenia	

Treatment: General Considerations

The primary-care physician is in the best position to treat most of the disorders that present with symptoms of the undifferentiated primary-care syndrome. The combined use of supportive suggestion and advice (the most commonly used of medical treatments), along with pharmacological control of prominent biological affective symptoms is in the best tradition of an integrative approach to treatment. This approach involves the normal clinical interviewing, diagnostic, and therapeutic skills of the physician (16).

The flow chart (Fig. 51.1) provides a decision tree for assisting in the selection of drugs that may be the most useful in the treatment of the undifferentiated syndrome, depending on which affect or affects predominate, chronicity of symptoms. Table 51.2 describes the pharmacological characteristics of medications used in the treatment of anxiety. See Table 50.1 for a listing of antidepressants.

In most cases, the following principles of conservative management provide the most effective outcomes:

1. Routine visits and screening.
2. Minimal but adequate prescribing.
3. Calm doctor—tolerance of anxiety.
4. Avoid iatrogenic dependency.
5. Judicious use of diagnostic testing.
6. Openness to surprise and to alternative diagnoses.
7. Assess risks; is the patient in danger; e.g., suicide, domestic violence.

The most powerful drug that can be administered is the personality of the doctor in the context of the medical setting (17). The literature supports the effectiveness of the verbal treatments most often dispensed by the doctor (13, 17). The combined use

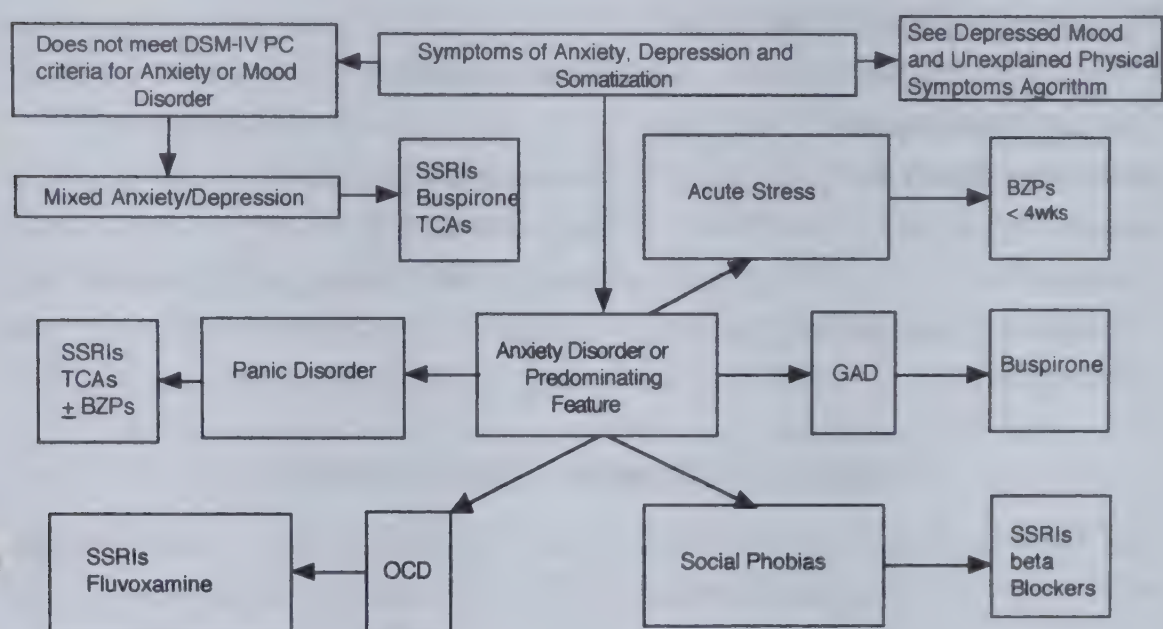


Figure 51.1. Flow chart for treatment of anxiety disorders or undifferentiated primary-care syndrome. BZP, benzodiazapines; GAD, generalized anxiety disorder; SSRI, selective serotonin reuptake inhibitor; OCD, obsessive compulsive disorder; TCA, tricyclic antidepressant. (Modified with permission from Lydiard RB. Coexisting depression and anxiety: special diagnostic and treatment issues. *J Clin Psychiatry* 1991;51(Suppl 6):48–54. Copyright 1991, Physicians' Postgraduate Press.)

of supportive suggestion along with medical control of the biological aspects of the illness is in the best traditions of an integrative approach to treatment.

If there is a failure to achieve the expected response to treatment (including the drug “doctor”), consider the following (18):

1. **Diagnosis:** Is something missing. This is an essential step, both in terms of selecting the correct treatment, but also in assuring the confidence of both doctor and patient, fundamental to the efficacy of verbal and drug therapy. Consultation or referral to a psychiatrist or other mental health specialist is often helpful here.
2. Is the dose either too low or too high, or of inadequate length? Inadequate dosing is the most common reason for failure of drug treatment.
3. **Switch drugs.** A drug in a different class or another drug in the same class may be more effective or better tolerated.
4. Are there cultural, racial, or ethnic factors that may affect understanding or communication between doctor and patient?

Table 51.2.
Antidepressant and antianxiety agents.

Antidepressant Agents								
Drug Class	Effects							
	Dose mg	Blockade of Biogenic Amines	Anticholinergic Effect	Lethality of Overdose	Sedation	Half-life (hrs)	Arrhythmia Potential	Drug Interactions
Tricyclics								
Tertiary Amines								
Amirypitiline	50–300	+	++++	High	+++	16	Yes	Many
Imipramine	50–300	++	+++	High	+++	18	Yes	
Secondary Amines								
Desipramine	50–150	+++	++++	High	+	18	Yes	Many
SSRIs								
Sertraline	50–150		++++	Low	Low	24	Low	Few
Paroxetine	20–50		++++	Low	Low	—	Low	Few
Fluoxetine	20–80		++++	Low	Low	120	Low	Many

NE, norepinephrine; 5-HT, serotonin; SSRI, selective serotonin reuptake inhibitor

Table 51.2 (continued).
Antidepressant and antianxiety agents.

Anti-anxiety Agents						
Drugs that Could Cause Dependence						
Drug Class	Effects					
	Daily Dose mg	Onset of Effects	Sedation	Half-life hrs	Comments	
Benzodiazapines						
Long-acting (half-life >24hrs)						
Chlordizepoxide	25–50	Intermediate	Yes	7–48	<u>not</u> effective in PD	
Diazapam	10–30	Fast	Yes	20–90	effective in PD	
Clonazapam	1.5–6	Intermediate	Yes	24–48		
Short-acting (half-life <24 hrs)						
Alprazolam	1.5–6	Intermediate	Yes	12–15	effective in PD	
Lorazepam	3–6	Intermediate	Yes	10–20	safer in elderly	
PD, panic disorder						
Drugs that are Free of Dependence						
	Daily dose mg	Onset of effects	Sedation	Half-Life hrs	Comments	
Azapirones (Buspirone)	15–40	Weeks	Low	2.5	Side effects similar to SSRIs; said to be less effective with previous BZPs	

SSRI, selective serotonin reuptake inhibitor; BZP, benzodiazapines

Panic Disorder

Panic disorder is distinct from generalized anxiety with a different course, different history, different genetics and demographics, and characteristic responses to specific drugs and certain chemical challenges.

A panic attack has a sudden onset, sometimes in the middle of the night, that lasts minutes. There is intense air hunger and massive autonomic arousal with pounding heart, butterflies, lightheadedness, sweating, flushing, tremor, tingling, and choking. In the course of the episode, the patient fears death, going crazy or losing control. There is a need to flee to a familiar setting, usually home, or to a familiar person. These patients may go to emergency rooms and from doctor to doctor. They often become housebound in order to avoid recurrent attacks. They avoid places where they have had attacks, and the scope of their lives becomes more and more restricted (14).

Panic disorder is twice as frequent in women, and it recurs over time, sometimes in clusters. It is the fifth most common clinical diagnosis you will make (17, 19). It may follow a loss, demands for more independent behavior or other stress, and it may result in a secondary generalized anxiety disorder or anticipatory anxiety (20). Agoraphobia is a major disability, even after control of the panic symptoms, such as in riding a bus or an elevator to get to your office. It is believed that this complication can be prevented or minimized with adequate treatment of the panic attacks early in the course of the illness.

Identical twins are 50% concordant for panic disorder and first-degree relatives have up to 18% concordance. Lactate infusion, yohimbine, and CO₂ all elicit panic attacks in those who have the disorder.

Panic disorder is the first of the anxiety disorders for which a specific effective drug treatment was found. Tricyclic antidepressants, which are believed to suppress a central noradrenergic trigger mechanism in the brain stem, were found to control the core symptoms of panic disorder. Subsequently, alprazolam, a high potency benzodiazapine, was also found to be effective in controlling the symptoms, implicating the GABA receptor system in panic disorder. More recently, with the finding that SSRIs are also quite effective as antipanic agents, the role of 5HT receptors have opened new avenues for research and understanding.

As the psychopharmacology of panic disorder is more understood, it becomes clear that it is a complex and probably biologically heterogeneous disorder. With the development of second-generation antidepressant medications and the implication of the many 5HT receptors in a variety of disorders, it now seems the new medicines transcend and perhaps redefine the boundaries of seemingly unrelated clinical syndromes (Table 51.2). "The diffuse connections of serotonin (Fig. 51.2) allow it to affect many basic psychobiological functions such as anxiety mechanisms and the regulation of mood, thoughts, aggression, appetite, sex drive, and the sleep/wake cycle" (20).

Psychodynamics of Panic Disorder

Panic disorder is most effectively treated initially as a neurophysiological disorder. Psychodynamic psychotherapy alone has not been effective in curing panic disorder and success rates are no better than would be expected due to spontaneous remission.

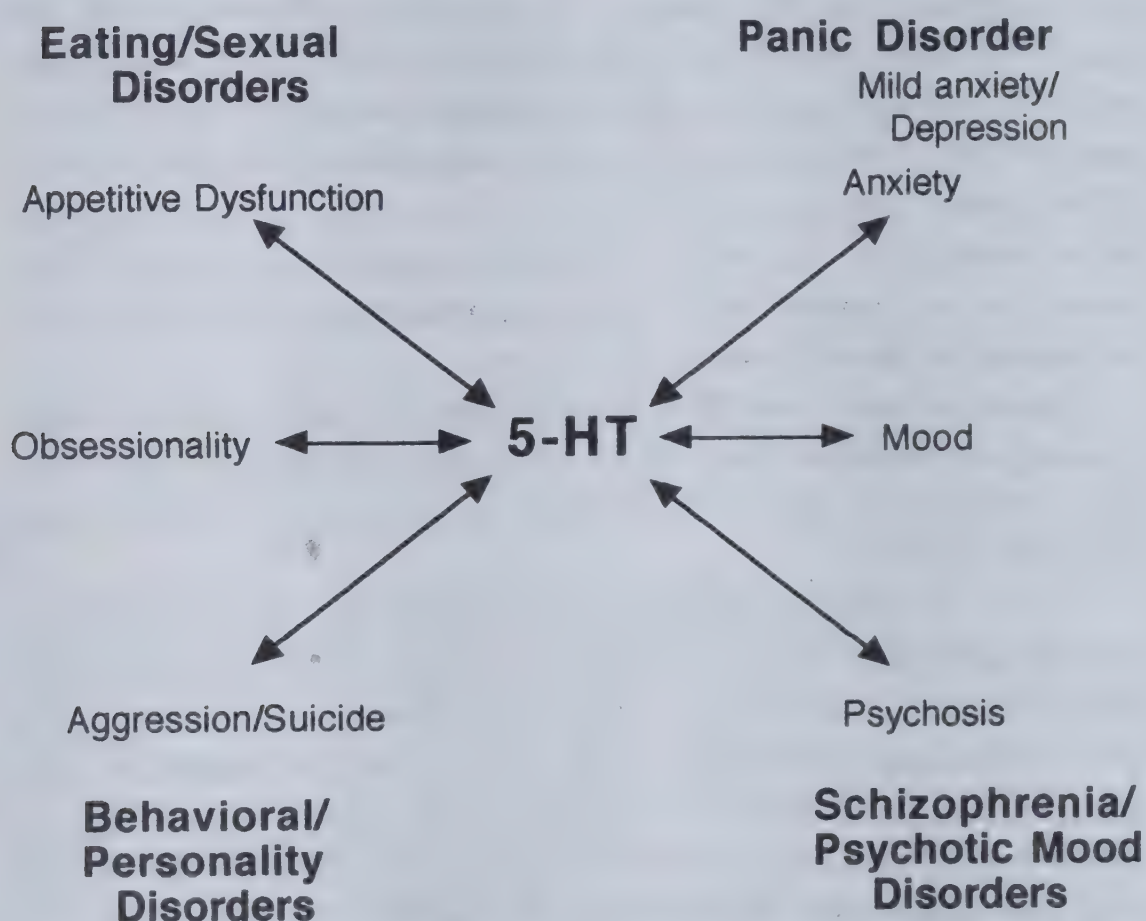


Figure 51.2. Serotonin and brain dysfunction. (Reprinted with permission from Dubovsky SL, Thomas M. Serotonergic mechanisms and current and future psychiatric practice. *J Clin Psychiatry* 1995;56(Suppl 2):38–48. Copyright 1995, Physicians' Postgraduate Press.)

However, the success of cognitive-behavioral therapy in treating panic disorder shows that a supposed psychobiological condition can be treated by psychological means alone. In cognitive behavioral therapy, the focus is on catastrophic misinterpretation rather than intrapsychic conflict (20) (see Chapter 49).

Once the core biological symptoms have been controlled through medication and support, a certain number of patients can benefit from insight-oriented, psychodynamic psychotherapy for secondary, predisposing, or coexisting characterologic or neurotic conditions. Indeed, most panic disorder patients probably benefit from a combined approach that includes neurophysiological, cognitive-behavioral, and psychodynamic elements (20).

Treatment and Prognosis of Panic Disorder (PD)

The treatment of PD is primarily medical, and the condition can often best be explained to patients according to the medical model. This will have the additional benefit of relieving some of the guilt and shame these patients have about losing control or being weak. The patient should be encouraged that with treatment, the symptoms can be cured.

The first line of medical treatment in the primary-care setting is the selective serotonin reuptake inhibitors (Table 51.2) (18). If symptoms are intense and disabling, a high-potency benzodiazepine such as a clonazepam can be used short term through the latency period that is associated with all antidepressants (Table 51.2).

Patients with anxiety disorders are exquisitely sensitive to side effects, so it may be necessary to begin medications at a very low dosage and slowly increase to therapeutic levels. I usually use either sertraline or fluoxetine and avoid low-potency benzodiazepines, which have no effect in PD. I no longer use alprazolam, due to long-term intolerance in the vast majority of patients, preferring clonazepam, another high potency, longer-acting benzodiazepine, to accomplish what is otherwise a protracted and difficult withdrawal (21).

Prognosis depends on such factors as age of onset, severity, and duration of symptoms and environmental, psychosocial factors such as stress and stability of personal life. Response to treatment is excellent, especially if begun before disabling phobic restrictions have emerged. It is important to remember that there is excess mortality in patients with PD, due to suicide and med-

ical conditions. It has been reported that up to 40% of patients presenting with anxiety have a medical cause for their symptoms (4,18).

The Phobias: Agoraphobia, Social Phobia, and Simple Phobia

The phobias, along with obsessive compulsive disorder, represent a manifestation of anxiety which unlike GAD or panic attacks, is bound to a situation, such as in agoraphobia, or social phobia, an object or a place, as in simple phobia, or to an idea, as in obsessive compulsive disorder (14).

Agoraphobia, both with and without panic attacks, is the most disabling of the phobias, while the social and simple phobias are usually not incapacitating, although they can be quite inconvenient. In its more severe forms, when associated with panic disorder, agoraphobia can be an extremely disabling condition, resulting in significant social and occupational dysfunction. The patient is usually afraid of being trapped in a situation where escape would be difficult or embarrassing due to anxiety, losing control through panic attack, fainting, or loss of bowel or bladder control (14).

Social phobia typically involves fear of situations in which the individual will be the subject of critical scrutiny by others. While the person recognizes that the fear is unreasonable, he/she often goes to great lengths to hide it and to justify the often elaborate tactics he/she must adopt to avoid certain situations. These may include public speaking, writing or performing in public or being in public places such as a church or restaurant where they might be humiliated before others. A patient may be unable to urinate in public or fear saying foolish things in front of others. Social phobias are often associated with other anxiety disorders, especially panic disorder (22).

Simple phobias are extremely common and rarely disabling. The list of phobic objects and situations is long. However, the most common involve snakes, blood, closed spaces, various animals. The phobic stimulus will almost invariably provoke anxiety, which decreases with distance from the phobic object or situation.

Most of these symptoms are familiar to psychiatrists and other mental health professionals, usually as they emerge in the course of treatment for other, more serious or incapacitating anxiety or depressive disorders.

Treatment and Prognosis of Phobic Disorders

These disorders are usually only mildly troublesome, and drug treatment is usually not necessary. Monoamine oxidase inhibitors, high-potency benzodiazapines, and selective serotonin inhibitors have all been used in social phobia. Behavioral therapy is often used for simple phobias. If the patient has significant disability, there is usually another mental disorder present requiring more specific treatment. Whatever treatment model is used, the patient must eventually be helped to face and master that which is feared.

Obsessive Compulsive Disorder and Chronic Anxiety

In this section we will discuss the more chronic and pervasive conditions. More often than not, they are associated with symptoms of other mental disorders, especially depression and other anxiety disorders. General anxiety disorder (GAD) is relatively infrequent as a single diagnosis and tends to merge with the personality disorders.

Obsessive compulsive disorder is especially interesting and has been the subject of a great deal of research interest and is yet another disorder linked to a serotonin mechanism (Fig. 51.2). The disorder is characterized by recurrent, persistent thoughts (obsessions), always unpleasant, often having to do with doing unspeakable things to loved ones, which the person attempts to suppress, ignore, or to neutralize by some action or undoing thought. The person recognizes that these thoughts are absurd and this contributes to his suffering since he or she is usually ashamed of his or her condition and may endure it for years (see DSM-IV PC, 14).

Compulsions are senseless activities that are performed in response to an obsession and include stereotyped rituals, hand washing, counting, which if resisted, lead to mounting discomfort and anxiety. The condition can range widely in severity from relatively mild to completely incapacitating. The disorder frequently is associated with other anxiety disorders and depression and merges with the personality disorders.

Psychodynamics of Obsessional Thinking

The classical psychoanalytic understanding of obsessional neurosis (which is distinct from obsessive compulsive disorder) is that the individual has regressed to an earlier form of thinking

and feeling in the face of feared retaliation for aggressive and sexual impulses. This means that all of the infantile wishes, impulses, aggressions, and lusts are obsessional, displaced to thoughts and fears that disguise the unconscious aims of the repressed impulses. The anxiety is thereby bound in the obsessional thoughts and rituals.

As a practical matter, such patients may at times be somewhat difficult to work with, due to their characteristic ambivalence, endless doubts, perfectionism, and concern with details.

Treatment and Prognosis: Obsessive Compulsive Disorder and Generalized Anxiety Disorder

The use of serotonin uptake inhibitors has been a major breakthrough in the treatment of obsessive compulsive disorder (Table 51.2), which suggests a neuropharmacological relationship to the other anxiety disorders, as well as to depression. Behavioral therapies have also been reported to be useful. However, expressive insight- or analytically oriented therapies are not effective in treating this disorder.

Generalized anxiety disorders are characterized by chronic worry and anxiety symptoms. Azopirones, which do not have the risk of dependency, have been demonstrated to be effective in treating anxiety, as well as mixed anxiety and depression, and should be the first choice (Table 51.2) (23). Verbal therapy is effective, and there is no measurable benefit to prolonged use of benzodiazapines in this condition.

SUMMARY

Undifferentiated Primary Care Affective Syndrome provides a way to identify mental disorders that supports and enhances those activities that set primary care apart from all other medical disciplines and settings. Anxiety, either as a disorder or as part of the undifferentiated syndrome, is one of the most frequent symptoms in primary care. We have seen that just as the neurochemistry of the anxiety disorders transcends diagnostic boundaries, so also does the patient and the illnesses that the doctor is called upon to treat. The doctor-patient relationship is the foundation. It is a unique system that accommodates the subjective and the objective, the psyche and the soma. The patient is always more than the sum of the diagnoses that can be applied. Our cate-

gories should support diverse functions of the doctor while maintaining the integrity of the patient.

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Somatic Symptoms without Organic Basis

Douglas M. Post and David R. Rudy

INTRODUCTION

It has been estimated that 40% to 60% of visits to primary-care physicians are by patients who manifest no biomedical basis for their somatic symptoms. Along with straightforward desire for information or alleviation of fears, a great proportion of these visits are for symptoms of somatization of psychological problems (1). Although they share the characteristic of physical symptoms with little or no organic basis, somatizing patients can be classified into distinct entities with separate diagnostic features, each responding to a different therapeutic approach. Some overlap between groups does exist, but for purposes of clarity, they will be presented independently. With appropriate diagnostic and treatment strategies of the various functional somatic disorders, somatizing patients are not stereotyped into a single group with a pejorative nickname such as "hysteric." Thus, patient care can be improved, physician and patient satisfaction enhanced, and health-care expenditures reduced.

The great majority of symptoms that patients bring to physicians are physical in nature. Some symptoms clearly yield to pathophysiologic analysis, while others do not. Nonconforming symptoms can occur in the absence of organic disease or be disproportionate to expectations from objective findings when organic disease is present. These are often referred to as functional symptoms or "functional overlay," respectively (2). This group of patients seems unable to express directly psychological or social distress.

As a group, they spend excessive amounts of time and energy searching for a physician who can cure their ills. Physicians often react negatively, and label patients as “rocks” or “turkeys” if exhaustive diagnostic testing reveals little, and when patients react negatively to attempts at reassurance. In one study, a group of patients with multiple office visits without objective findings spent an average of 7 days ill in bed each month, and accumulated remarkably high health-care charges (3). Others have noted the lack of appropriate mental health services for somatizing patients who over-utilize primary care as a threat to the financial viability of the health maintenance organizations (4).

SOMATOFORM DISORDERS

The diagnosis of a somatoform disorder describes a presentation of physical symptoms that cannot be explained by a diagnosable medical condition (5). DSM-IV has clarified this classification after previous diagnostic manuals, and has included the following subtypes: Somatization Disorder, Conversion Disorder, Pain Disorder, Hypochondriasis and Body Dysmorphic Disorder. [One could add also the Stress Disorders, since they may lead to psychophysiological dysfunction wherein symptoms are “real,” i.e., not somatized, yet devoid of organic change (e.g., tension headache).] This chapter will not deal with psychophysiological disorders that produce organic disease, such as peptic ulcer disease and bronchial asthma.

Somatization Disorder

This entity pertains to a set of chronic, subjective complaints that generally has an early onset and perseveres over many years. Somatization disorder is prevalent and could be diagnosed daily in a full practice (6). Three common features that suggest somatization disorder versus a general medical condition include: 1) multiple organ system involvement; 2) early onset, usually adolescence, and chronic course, and 3) absence of ancillary testing abnormalities that are typical of the suggested medical condition (5).

Cloninger (7) has suggested a set of four symptom clusters related to this disorder: a history of medically unexplained pain in at least four different parts of the body, two or more gastrointestinal symptoms other than pain, at least one symptom that is sexual or referable to the reproductive system, and at least one conversion symptom.

Patients with somatization disorder present with an affect that does not match the implications of the symptoms(s), but they may “wear” the illness much as a badge of office. Frequently, they carry a tale of purported incompetence of a line of preceding physicians, none of whom allegedly appreciated the patient’s suffering nor took an interest. As stated, informing such patients in too direct a manner that the tests are normal, hence that nothing is seriously wrong (heard as “nothing is wrong and this must therefore be all in your head”), may lead to angry outbursts.

For somatizing patients, healing can be promoted if the physician initially acknowledges the patient’s discomfort and illness. These patients tend to be motivated by the pursuit of a caring relationship, and this acknowledgment, which will likely be contrary to previous experiences with physicians, can be a helpful building block to the formation of a productive therapeutic alliance. Explaining that somatization is a medical disorder that runs in families and that does not cause physical decline can be beneficial (8).

Structuring regular visits that are not dependent on the patient being symptomatic is also useful. To schedule a “return as needed” visit encourages the development of new symptoms. Initially, the physician may tend to order more studies than appear necessary. However, psychologically, medical testing serves a protective mechanism that patients have learned to use as a maladaptive response. Further, it certifies the physician’s serious approach to the patient’s symptoms and renders the patient more receptive to later counseling approaches (8).

Doctor-patient communication is essential. Positively reinforcing nonillness, i.e., normal, dialogue and talking with the patient in a way that reduces the possibility of the message being interpreted as a rejection can be effective interaction strategies. It can also be advantageous to both physician and patient to form realistic treatment goals. Physicians should not expect a cure nor the total disappearance of symptoms (9).

Conversion Disorder

Diagnostic criteria for conversion disorder include the presence of one or more symptoms affecting voluntary motor or sensory function that cannot be completely explained by a known medical condition, as well as a discernible relationship between psychological

factors and the manifestation of symptoms (5). Motor symptoms or deficits include impaired coordination or balance, paralysis or localized weakness, difficulty swallowing, and urinary retention. Sensory symptoms include loss of touch or pain sensation, double vision, blindness, and deafness. Pseudoseizures may also be involved (10). Symptoms tend not to correspond to common anatomical and physiological models, but will coincide with the patient's concept of his or her condition. A diagnosis of conversion disorder should be made only after the performance of a thorough medical evaluation and should be considered tentative, since medical conditions, such as multiple sclerosis, can take years to develop into distinct diagnostic entities. These patients generally receive, and often warrant, at least baseline EMGs, EEGs, and CT scans of the brain and spinal cord.

Conversion disorders are distinguished from somatization disorders by their acute and episodic nature, their distinctive character, and by patient presentations of only one complaint. Conversion disorder symptoms may be present at any age, but they tend not to occur before age 10 nor after age 35. Recurrence is common (11).

Conversion disorders present with a nonverbal demeanor that often seems not to fit the seriousness of the complaint. For example, there may be a complaint of abdominal pain that persists over several visits despite negative historical and physical, as well as sigmoidoscopic and possibly barium enema findings. The patient appears not to be terribly bothered by either the degree of pain nor the diagnostic possibilities. She or he may answer only vaguely a direct question as to whether she is afraid of the possibility of cancer. This has been referred to historically in medicine as *la belle indifférence*, or a calm indifference to the implications of the symptoms.

A conservative, suggestive approach is recommended for patients with conversion disorders. Telling the patient that symptoms are psychogenic in nature will often result in an exacerbation of symptoms. Patients often respond well to suggestive approaches, however, such as informing him/her that the symptom seems to be one that will resolve rather quickly (8). Factors that tend to be associated with a good prognosis include an acute onset, the presence of specific stressors at the time of onset, a short time interval between onset and treatment, and above-average intelligence in the patient (5).

Pain Disorder

In this, pain is the predominant focus of the clinical presentation and is viewed as causing significant distress in one or more important areas of patient functioning. Psychological factors play a significant role in the onset, severity, exacerbation, and/or maintenance of the pain. These may include issues of litigation at a secondary level. Many physician evaluators are referring to these patients when they use the term "compensation neurosis." This refers to a tendency for pains ostensibly caused by industrial injuries to be steadfastly persistent, only to quickly subside after the compensation issue is settled. Ten percent to fifteen percent of U.S. adults have at some time a degree of work disability due to back pain alone (5).

The course of pain disorder is affected by a number of variables. It is often associated with other mental disorders. Chronic pain appears to be most frequently associated with depressive disorders, whereas acute pain seems to be affiliated more often with anxiety disorders. The mental disorder may precede the pain disorder, occur simultaneously with it, or result from it. Both the acute and chronic forms of pain disorder are frequently associated with insomnia (5).

Communicating an empathic understanding of the patient's pain is a useful first step in management. The patient should be informed that the treatment goal is not necessarily a pain-free life, but a process of adaptation and rehabilitation. Interdisciplinary approaches have demonstrated treatment efficacy, encompassing modalities such as medication, physical therapy, biofeedback, cognitive therapy, pain control programs, and psychotherapy (12). Many patients present already addicted to outpatient narcotics such as codeine and its congeners and propoxyphene. Pain clinics are useful referral services to avoid the trap of prescription escalation.

Hypochondriasis

The diagnosis of hypochondriasis involves an obsessional fear that one has a specific serious disease though the perceived disease may change from time to time. Thus, while pain disorder focuses on the symptom, hypochondriacs fixate on a diagnosis. Recent formulations have characterized this disorder as a cyclical process. The first step involves a selective focusing of attention on

a somatic symptom that is typically benign. Next, the perception is labeled as a health emergency and catastrophic threat. The patient then experiences the anxious belief that urgent attention and treatment are needed, and a visit to the physician or emergency room occurs. As a final step, the anxiety cycles back to a heightened focusing on a somatic sensation, generally leading to intense disease anxiety on the part of the patient and mutual exasperation for both patient and physician (13).

Treatment for hypochondriacal disorders includes assessment of comorbidity with depressive and anxiety disorders. For example, hypochondriasis may be a symptom of depression, which must be treated. As with most other somatoform disorders, patients with hypochondriasis are not reassured by testing that reveals an absence of organic pathology and similarly, the establishment of a therapeutic alliance is an instrument of healing. It has been suggested that providing these patients with a diagnosis to which they feel entitled, such as "syndrome of neurologic amplification of body sensations," can reduce the tension in the doctor-patient relationship and lead to improvement (8).

Other modalities include cognitive-behavioral techniques, particularly in a group treatment setting. Helping patients to modify their distorted interpretations by realistically examining all the evidence and facilitating the discovery of non-threatening explanations for their symptoms are useful cognitive strategies (14).

DEPRESSION

Studies have proposed that approximately three-fourths of patients with depressive disorders are evaluated by primary-care physicians (15). One-half of these disorders are either unrecognized or misdiagnosed in pure psychiatric criteria, though a great percentage may go tacitly unacknowledged by physicians, perhaps appropriately so. Many may be examples of the "undifferentiated primary care syndrome" of Ronning (see Chapter 51). Be that as it may, the proportion of significantly depressed patients truly missed by physicians leads to poor individual functioning and expense (16).

One factor related to the problem of detecting depression is that the majority of depressed patients bear a physical symptom as the chief complaint. These may include the typical

symptoms associated with depression, including sleep disturbance, appetite changes, fatigue, psychomotor retardation, diminished sexual desire, and concentration difficulties. Other presentations of depression include nonspecific cardiopulmonary and gastrointestinal complaints, or problems with localized pain, such as headache (17). Thus, the depression may be “masked” by the somatic symptoms, which are coping mechanisms to deny or minimize the feelings associated with depression, or the somatic symptoms may be “offerings” to initiate and to test the patient-doctor relationship. Problems with social and/or family stigma, insurability, and confidentiality may also contribute to the infrequent presentation of depression as the chief complaint (18).

The patient with somatized depression, as those with somatization and conversion disorders, carries a demeanor that does not match the implications of the symptom. However, rather than exaggeration or indifference, the effect is more likely one of distraction or fatigued preoccupation. For example, the patient, perhaps a 45-year-old male, may complain of chest pain. However, the body language conveys, rather than fear and anxiety, lest he may be suffering from a coronary event, a sense of flatness. When asked what he fears may be the cause of the pain, he may seem to be vague. If asked to point out the location of the pain, he will not show a doubled fist over the sternum with appropriately anxious facial expression, but may press gently with one finger over the heart area. Similarly vague pointings will accompany abdominal pain, otherwise poorly described. This somatization of depression has been called *somatic depressive equivalent*. When sensing this presentation the physician should not hesitate to investigate for depression, e.g., with direct inquiry regarding the patient’s mood and questions regarding early awakening.

Coexistence of depression with major medical disorders may also present detection problems to the busy family practitioner. In patients with selected but common chronic illnesses, studies have indicated prevalence rates of depression in the 25% to 50% range (19). These diseases include diabetes mellitus, cancer, stroke, Alzheimer’s disease, and coronary artery disease. Addressing both the psychological contributions and the organic disease process will facilitate a more rapid favorable outcome.

Regarding treatment, research through the National Institutes of Mental Health have indicated that combined drug treatment and psychotherapy for patients with major depression is the most effective (20). Pharmacologic approaches are covered in Chapter 50.

ANXIETY

Anxiety is a common symptom in the primary-care health setting. It has been estimated that approximately 20% of typical family practice patients have a clinical anxiety disorder (21). As with depression, patients with an anxiety disorder often present to physicians a physical symptom that they may not associate with the affective state. Often, the presentation consists of a multitude of symptoms: chest pain, hyperventilation, tachycardia, palpitations, dizziness, nausea, headache, diarrhea, and abdominal pain.

Anxiety may be a result of fear of the implications of a symptom such as chest pain or the state of anxiety may be somatized as with depression. In the former case, typically a person may have learned of a heart attack or the diagnosis of cancer in a friend or coworker. Out of suggestibility or, perhaps because of the physiology of hyperventilation, the patient has developed chest pain and readily voices fears of its implications. If heart disease is ruled out, he is rather easily counseled and reassured. In the case of primary anxiety, symptoms may be psychophysiologic as in hyperventilation or in sinus tachycardia or may include feelings of unreality due to increased circulating catecholamine levels. Patients' resistance to a nonorganic diagnosis is mild and short lived in anxiety somatization, compared with conversion or hypochondriac somatization disorders.

An underlying medical disorder may also mimic or coexist with an anxiety disorder. Consumption of caffeine, cocaine, amphetamines, theophylline, beta agonists, over-the-counter decongestants, steroids, and marijuana can exacerbate anxiety or precipitate panic attacks. Cardiovascular disease, hyperthyroidism, pheochromocytoma, temporal lobe epilepsy, inner ear disease, hypoglycemia, and mitral valve prolapse should also be considered in the differential diagnosis of anxiety.

Treatment for anxiety parallels that of depression, in terms of combined psychotherapeutic and pharmacologic approaches. Therapeutic techniques include cognitive therapy, meditation, biofeedback, systematic desensitization, and cognitive behavioral

approaches. Recently, increased attention has been directed to the use of SSRIs in the pharmacologic management of patients with anxiety disorders as a means to reduce the side effect profile associated with some anxiolytics, and to eliminate the addictive properties of others. Anxiety is dealt with in detail in Chapter 51.

Table 52.1. demonstrates the relationship of nonorganic somatic symptoms to various mental disorder diagnoses.

MALINGERING AND FACTITIOUS DISORDERS

Malingering describes a pattern of behavior in which the patient consciously presents a set of plausible somatic symptoms as a means to attain some type of secondary gain (5). Malingerers pretend to be sick in their attempts to achieve secondary gains. Malingering may be adaptive at times, as when a victim of domestic violence uses a strategy of feigned illness to escape a violent home environment.

Malingering should be suspected when the patient presents one or more of the following circumstances: 1) a medicolegal implication; 2) noncompliance with treatment and an overall lack of cooperation during medical visits, and 3) the presence of antisocial personality disorder (12). If possible, it can be helpful to reduce the positive reinforcement that often accompanies the role of the malingering ill patient. Alertness to this condition is

Table 52.1.
Nonorganic somatic symptoms and psychiatric diagnoses.

Anxiety or depressive disorders	Usually one or two somatic symptoms of acute onset and short duration
Panic disorder	Somatic symptoms experienced only during panic episode
Hypochondriasis	Patient's focus is on the fear of a disease, not focus on a symptom
Pain disorder	One or two unexplained pain complaints, symptom fiercely defending
Conversion disorder	Only one or two motor or sensory complaints, often with neurologic implications
Somatization disorder	Lifetime history of multiple complaints

Adapted from Guggenheim FG, Smith GR. Somatoform disorders. In: Kaplan HI, Sadock BJ, eds. Comprehensive textbook of psychiatry. 6th ed. Baltimore: Williams & Wilkins, 1995:1251-1270.

necessary to avoid over utilization and to intercept attempts at fraud.

Factitious Disorders

Factitious disorders are similar to malingering, in that the patient intentionally assumes the sick role and presents symptoms to meet certain psychological needs. However, there is no apparent overt secondary gain involved in a factitious disorder (5). Personality disorders and significant difficulties in interpersonal relationships are frequent coexisting conditions. Vague and dramatic patient histories and departure from the hospital against medical advice are also fairly common entities. Munchausen's syndrome is a subgroup of the factitious disorders, and is characterized by pathological lying and wandering from hospital to hospital with the goal of admission and protracted stay in the inpatient environment (22). As originally described, it was applied to patients seeking surgery, but in usage it relates to medical treatments as well. Humane patient management and adjusting treatment goals from "curing" to "caring" are beneficial strategies, so long as the errant behavior is not reinforced.

Stress Disorders

These disorders feature many manifestations that are not necessarily characterized by somatization, such as traumatic stress disorder. On the other hand, stress disorder features several somatic symptoms that are not caused by organic abnormality but rather by physiologic dysfunction, such as tension vascular headache and irritable bowel syndrome. In these syndromes, the patients are quite likely not to be psychiatrically diagnosable but may find themselves in stressful situations ranging from fatigue and burnout associated with scholastic examinations or preparation of reports to separation, divorce, and empty nest syndrome. They are usually concerned with the severity as well as the significance of the symptom. These patients may respond well to rational cognitive counseling and biofeedback, rarely exhibiting resistance to acceptance of a diagnosis of "functional" disease.

FAMILY AND CULTURAL FACTORS

Family factors have been found to be influential in the production and maintenance of somatizing behavior. Some families lack

language for emotional expression, some directly discourage feeling-oriented statements, and some give attention solely to physical, nonemotional pain. Children growing up in these types of families learn to avoid, deny, and suppress emotional pain, and may amplify somatic symptoms to get their needs met (23). Minuchin (24) has suggested that psychosomatic families have distinct attributes: enmeshment, rigidity, poor conflict resolution, overprotectiveness, and a tendency to triangulate one of the children. Family and somatization patterns can mutually maintain and reinforce one another, creating a circular process.

Attending to these family characteristics and working with the somatizing patient through a family systems approach may pay satisfying dividends. A variety of family-oriented strategies has been suggested: collaborating with the family and eliciting their support in solving the mysterious aspects of the patient's illness; taking a genogram and examining transgenerational patterns that may be contributing factors; identifying role changes in the family, and writing a "prescription for illness" with the family, in which the patient and each family member specify what they would have to do to produce or exacerbate the patient's symptoms (25). This is addressed in Chapter 53.

These approaches are well within the expertise of the family physician, and considering the resistance to emotional explanations of symptoms, the family physician is in an ideal position to intervene. Professional collaboration can be extremely useful in this area, ranging from verbal consultation with a medical family therapist to direct involvement by the therapist with the family. If a therapist is directly involved, introducing that person as one "who has a special interest in working with mysterious medical problems" is much more effective than the consultation of a "mental health specialist" (25).

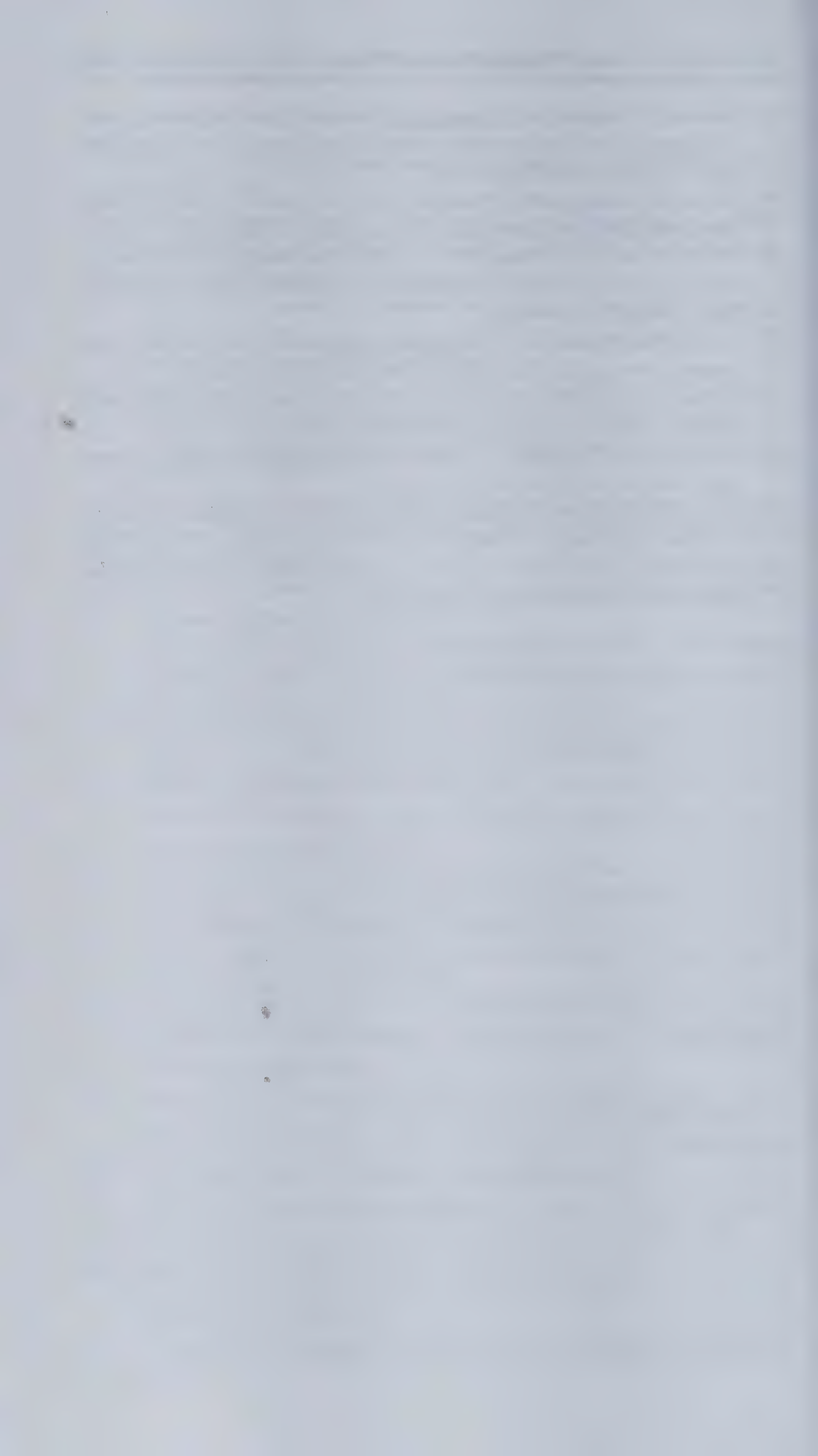
As with families, some cultures are prohibitive toward the direct communication of feelings, so that somatization may serve to indirectly communicate psychosocial difficulties. In this context, symptom profiles of patients from Italian cultures would likely be quite different from patients of Asian cultures.

Family physicians can greatly benefit from paying close attention to family and cultural factors in the patient presentation of symptoms. Patients are taught a great deal about interactions with health-care providers by their families and their culture, and will follow these "rules" of engagement in the medical encounter.

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Family Systems

Roger W. Schauer

THE SYSTEMS CONCEPT

The intent of this chapter is to identify the role for systems theory in family medicine, introduce systems theory and terminology in context of a case study, and briefly examine some systems therapy techniques.

INTRODUCTION TO SYSTEMS

The term *family system*, a relative newcomer to family medicine, is a theoretical framework that attempts to explain the effects of reciprocal interactions between individuals in a group, with "family" being the focus of those explanations. Systems theory addresses health and health seeking behaviors, in addition to behavioral and emotional/mental problems that affect individuals and their families. Properties ascribed to physical systems apply readily to interactions between individuals and groups, with similar use of terminology. A system, an orderly combination or arrangement of parts into a whole according to some rational principle, is different than the sum of its parts. Systems follow rules for interactions, and have properties such as boundaries, adaptability, and flexibility. Systems are dynamic, changing over time, and are in constant interaction, within and without. If left alone, a system tends to stabilize. If homeostasis is disturbed in any way, the system attempts to establish a new status quo. As participants in dynamic systems, individuals seek health-care services when their status quo is changed, when homeostasis is disturbed by an apparent health-related problem.

Biopsychosocial Model and Systems Theory

In his elegant and eloquent 1977 paper, George Engel advocated for a biopsychosocial model for medical care, and advanced the need for a new paradigm in medicine with his declaration that “a medical model must also take into account the patient, the social context in which he lives, and the complementary system devised by society to deal with the disruptive effect of illness” (1). Nearly two decades later, Inui, discussing the findings of the Pew-Fetzer Task Force on Advancing Psychosocial Health Education, confirms Engel’s contention (2). The Task Force, whose focus was relationship-centered care, described the need for mutuality between patients and clinicians, between practitioners and the community, and among the community of practitioners. Systems theory allows for the integration of the patient, the social environment of the patient and family, and the role of health-care providers. An understanding of systems helps us define our role as providers, improve relationships with patients, provide more holistic care, and generate efficient collaboration within the health-care team.

CLINICAL APPLICATION—LARRY’S PROBLEM

Larry was 10 years of age when his mother brought him to the clinic with a chief complaint of having soiled his underwear on a daily basis for the previous 3 weeks. The soiling occurred at school, at home on weekends, and during the night. History was negative for recent febrile illnesses, nausea, vomiting, or hard, explosive, or watery bowel movements. Past medical history was unremarkable, with immunizations current, normal growth and development parameters, and no previous incontinence problems. He interacted well with other children, earned average grades, and had no identified behavior problems. Parents and three younger siblings were in good health. Mother denied concerns about family stresses or problems. Physical examination was remarkable for fullness in the left lower quadrant, but absent of tenderness, rigidity, guarding, rebound, or abdominal wall or inguinal hernias. Visual examination revealed fecal-stained underwear and feces in the buttock crease, while digital exam revealed a rather large, firm fecal mass, with brown, occult negative stool.

The working diagnosis was encopresis due to fecal impaction with secondary overflow incontinence, and habit constipation.

After discussion with Larry and his mother, the fecal impaction was cleared by digital removal and oil retention enemas. A high-fiber diet, stool softeners, and increased oral fluids were recommended, with additional instructions to attempt to develop regular bowel habits by having Larry sit on the stool at the same time on a daily basis. An appointment, with request that the father also attend, was scheduled for 1 week later.

At the return visit, there was no change in the problem. Father was now also present, and the question of family stress was again raised. Family discussion revealed that there were serious financial concerns because they had lost much of their crop to hail and were in danger of losing their farm. Father felt he was under a great deal of stress and had been extremely demanding of his wife and children. During the visit mother suggested that father “quit hollering” at Larry. Father apologized to Larry for his own response to the stress, and the visit was terminated. The encopresis resolved with no recurrence.

EDUCATING PHYSICIANS ABOUT FAMILIES

Health-care literature that addresses teaching and training physicians about family systems has been meager, until recently (3). Doherty and Baird introduced a training model to evaluate levels of physician involvement (LPI) with families (4). Table 53.1 is a condensation of the cumulative knowledge and skills required for progressively greater involvement with patients and families.

The first visit for “Larry’s problem” was an LPI-1 encounter, as it dealt only with medical issues. The second visit, by including both parents and the identified patient, provided an opportunity for change because the three major individuals involved with the problem were present and heard the others’ stories. This LPI-3 encounter had a medical/social acceptable outcome, although no significant attempts were made to change basic family interaction patterns. While it presented as a medical issue, Larry’s problem was, in retrospect, a spousal problem brought to attention by Larry’s physiologic state.

TERMINOLOGY

Like most disciplines, family systems has developed its own language. Whether the physician becomes involved directly with family therapy, through collaboration with a systems therapist, or in-

Table 53.1.
Levels of physician involvement (LPI).

Level	Knowledge Base	Required Skills
LPI-1	Baseline bio-medical; routine training	Routine medical evaluation and technical skills required for patient care
LPI-2	Understanding for patients' learning styles, information needs, resources, and triangular dimension of physician-patient-family relationships	Communicating medical findings and treatment options to family members; soliciting patient & family opinions about the problem; changing interventions & referral decisions based on feedback from patient and family
LPI-3	Normal family development, reactions to stress, behavior, and illness; general systems theory; cultural issues	Empathic questioning & listening; integrating psycho-social issues with biomedical model; educating & encouraging family effort to deal with the problem; identifying family dysfunction and appropriate referral
LPI-4	Family systems or another counseling model for assessment and intervention	Structuring family meetings to engage even reluctant member participation; reframing problem definition to allow for alternative interventions or outcomes; identifying severe dysfunction & orchestrating referral
LPI-5	Systems and patterns for interaction with the larger system in cases of severe dysfunction	Interviewing families in conflict; dealing with family resistance to change; brief, strategic, or structural therapy negotiating collaboration with other professionals working with the family

Adapted from Doherty and Baird models (4).

directly by referral to therapists, an appreciation of terminology will facilitate communication with the patient/family and the referral network. A knowledge of systems terms may be of value to physicians, not because of pathologic descriptions or diagnostic value of the terms, but to recognize that these terms may describe mechanisms for survival or coping for individuals and families.

Interdependence

Family interactions become repetitive and predictable over time. These unwritten (and often unstated) rules about interactions may lead to negative consequences for one or more individuals in the system, but the rules are not challenged because they may not be recognized from within the system (5). Reciprocal interdependence, or feedback loops, plays a role in developing repetitive patterns of interaction, including those judged dysfunctional. Dysfunctional patterns can help the system maintain its status quo. Over time these patterns become ingrained, making it difficult for anyone within the system to visualize an alternative reality.

Larry's problem, while dysfunctional for him, helped the family system maintain its status quo because the parents were forced to pay more attention to his problem, with less time and energy expended on couple issues.

Boundaries

Healthy families foster individuality and balance closeness and distance. Boundaries define what is considered acceptable or unacceptable behavior and interactions, both within and without the family, and can be defined by permeability, ranging from excessively permeable to rigid or impervious (5–7). When boundaries within a system are excessively permeable, individual distinctions may become blurred, and the system is said to be enmeshed. While there is concern about potential negative consequences of enmeshment, some families or family members may adopt this mode as a survival or coping mechanism, especially if individuals feel they have not been protected by the larger system.

Rigid boundaries tend to isolate individuals within the family system, or families from the larger system. Individuals within families may be isolated and have rigid personal boundaries, which might prevent change, or even access to health-care activities. In families where boundaries are closed, the physician may find extensive resistance to suggestions for change in health-care behaviors. Families in which there are abusive relationships tend to have rigid boundaries. In some situations it may be detrimental to the individual or family system to simply identify and expose those boundary issues if the system doesn't have an alternative safe method of survival. Recent publicity has demonstrated

the failure of the larger (legal and protection) systems to provide for the needs of victims in families who do reach beyond the boundaries in search of help. When physicians recognize boundary problems, they may be able to appropriately intervene or refer the patient/family for appropriate help. We need to understand and respect the patient/family frame of reference.

For Larry's problem, boundary issues came into play at several levels. While the family boundaries were adequately permeable to seek outside help, there was also an initial resistance to acknowledge the stress level present in the family, even though the mother was asked about the possibility of stress being related to the presenting problem.

Triangulation

Counseling literature frequently refers to dyads and triads. Usual interactions involve two individuals (dyad), but family functions can assume a number of configurations. In family relationships with undue stress on a dyad, there is a tendency to involve a third person or activity (5, 8). Physicians frequently are called when that third person starts exhibiting the signs of illness or dysfunctional behavior. When the relationship between parents is dysfunctional, children (frequently unwittingly) help reduce the stress in the parental dyad by developing a problem. A child who has brittle diabetes mellitus, or episodic or chronic asthma, may become worse when his parents are fighting. If both parents become concerned about the child, or at least one of the parents takes the child to the emergency room, the fighting between the two parents stops and the child has learned how to temporarily "fix" the problem. Obviously we can not blame all problems or worsening of chronic problems on the effects or benefits of family interactions or triangulation. However, the potential for family dysfunction deserves consideration when individuals manifest recurrent, persistent, or recalcitrant problems.

Larry's problem can be viewed as the result of triangulation, where Larry became the third point in that triangle. Because the parents were forced to focus on his problem they had less time and energy for their conflict about their financial status. When the parents recognized this, and the father was able to retreat from his verbal attacks, Larry was able to resume his normal role as a child.

Reframe

Individuals and families dealing with a problem frequently can see only one cause or one potential outcome. Reframing or redefining a problem changes the context of the problem or situation and allows for alternative outcomes. Reframe is a technique employed in strategic therapy. A similar concept or technique employed by therapists is "restorying," or viewing the problem from an alternative reality. When Larry's medical problem could be seen as externally induced, by stress within the family, it no longer was a problem of regression or loss of continence.

Externalizing the Problem

Similar to reframe, externalizing the problem allows for solutions or suggestions for change that may be more palatable to the troubled system. If the problem can be defined in terms of outside influences rather than an inherent defect within the individual or family, there is less self-blame.

SCHOOLS AND TOOLS

Pioneers in systems therapy developed varied techniques as they explored methods to create change or unbalance in families where ingrained patterns of (dys)function created problems. Often charismatic, these individuals mentored other therapists with subsequent evolution of models or schools of therapy. More recently therapists have pursued training in various schools, sometimes developing eclectic approaches that may be less well defined but better fit the personality of the individual therapist. The following discussion highlights the basics of some of these models.

Strategic Family Therapy

Goals of strategic therapy are to change the perception of the problem or the solution. This requires an understanding of the reciprocal nature of behavior and the context and meaning of the behavior (6, 9). Change is imperative to effect a different outcome, and that change can be first order or second order. When change occurs within the system, *according to rules of the system*, it is described as first-order change. Second-order change occurs *when the rules of the system change*, resulting in change in the system

itself. Strategic therapy may consider the apparent logical solution as part of the problem.

For Larry's problem the goal of the family was to stop the incontinence. The family was stuck, as they had already depleted their arsenal of resources in their unsuccessful attempt to resolve the problem. A second-order change, a deviation from the usual patterns of interaction within the family, quickly allowed Larry to resume normal bowel control when bowel control was no longer the family focus. Strategic therapy requires the introduction of new information into the system so individuals can see things differently (reframing; restorying).

Structural Family Therapy

Structural therapy attempts to alter the structure that supports the problem. Structural systems theory grew from the recognition that the structure and organization within systems is determined by patterns of interaction within those systems. Family hierarchy is viewed in terms of the structure, subsystems, and boundaries within the family. Structure emanates from generic and idiosyncratic constraints. Generic constraints refer to the observation that all families have a hierarchical structure, described in terms of the roles of parents and children and supported by reciprocal and complementary functions of each individual in the system. Idiosyncratic constraints are those rules and patterns of behavior that are assimilated by individuals in their family of origin or other learning experiences. These rules and patterns are carried by individuals into their new system, their current family (6, 10). Subsystems are defined as spousal, parental, and sibling subsystems. Boundaries and rules of subsystems determine the family hierarchy.

Structural approaches to family dysfunction attempt to alter patterns of interaction that are deemed dysfunctional by modeling an alternative structure. During a family therapy session a structural therapist might ask individuals to exchange chairs in an attempt to model appropriate subsystem communication. If a child has become parentified (a frequent scenario when couples are fighting or divorced), the therapist might ask the parents to talk directly with each other, moving the child(ren) to another part of the room. In this case, Larry's problem, once externalized and reframed as a spousal subsystem problem, was resolved by the parents talking directly to each other, rather than through Larry.

Brief Therapy

Brief therapy is time-limited and focused only on those issues requiring an alternative outcome, as defined and agreed upon by the individual/family presenting the problem (6, 11, 12). Larry's problem was resolved in two visits, the first visit prolonged only by the misguided physical intervention, while the second visit was concluded within 15 minutes.

Genograms

Genograms, family pedigrees, family trees, or genealogy charts have long been used by physicians to record inheritable medical conditions. Genograms are time and space efficient, can quickly be reviewed in the family or patient chart, and, as family structure changes, can be appropriately updated with minimal or no narrative addition to the record (3, 13). They are of value in demonstrating family trends or problems of unknown etiology, such as divorce, mental illness, alcoholism and other addictions, and suicide or other untimely deaths. With the use of symbols, genograms can demonstrate chronic illnesses, relationships, and family discord, as well as identify those individuals sharing a household. Genograms permit visualization of family patterns, and provide opportunities to discuss alternative outcomes to chronic or recurring medical, emotional, or relationship problems.

Larry's family of origin, as seen in a genogram (Fig. 53.1):

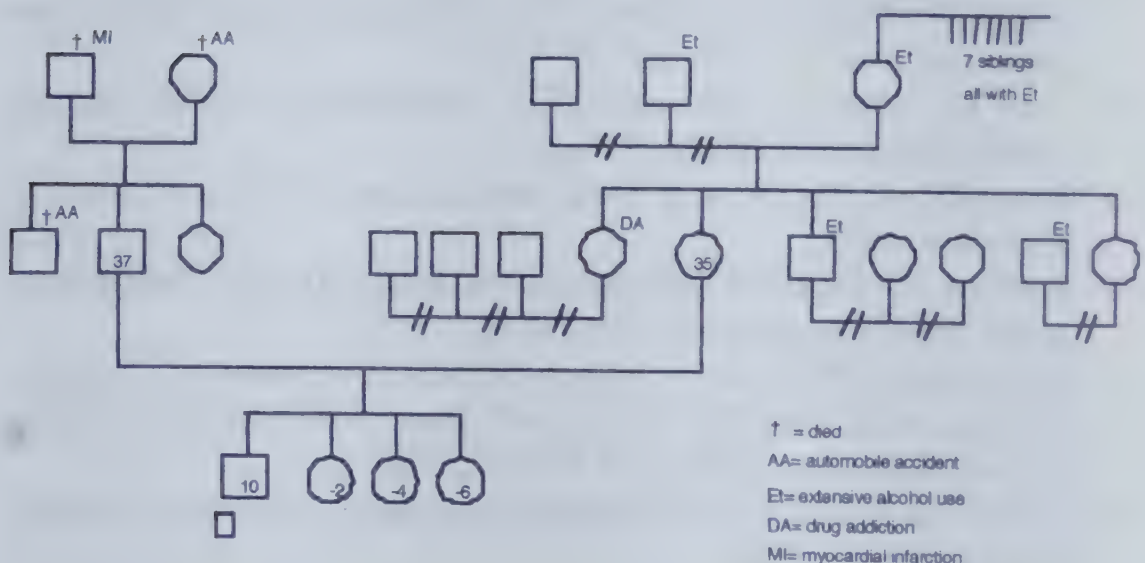


Figure 53.1

Larry's parents had learned different styles of parenting from their family of origin. Larry's father completed adolescence with an authoritarian father after the auto accident of the paternal grandmother. Larry's mother grew up in a family with multiple drug and alcohol problems, and without a present male role model. Divorce and abandonment became an acceptable method of conflict resolution.

Life Cycles

Life cycle models identify development tasks of individuals and families (3, 11). When individual development tasks are in conflict with family rules or family development tasks, this conflict can manifest itself as physical illness, emotional or mental illness, or dysfunctional behavior. With a comprehension of development milestones and issues and because of their intimate and systemic relationship with the family, family physicians have multiple opportunities for proactive or interventive strategies.

SUMMARY

Systems theory is a tool to aid family physicians as they address the bio-psycho-social needs of individuals and families. Systems allow for collaboration, with individuals, with families, and with the larger community, as physicians fulfill their mission to provide comprehensive, continuous, cost-effective, compassionate, and quality care.

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Recommended Childhood Immunization Schedule, United States—1996

Vaccine	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	4–6 years	11–12 years	14–16 years
Hepatitis B (Hep B) ^{ab}	Hep B-1		Hep B-2		Hep B-3					Hep B ^b	
Diphtheria, tetanus, pertussis (DTP) ^c		DTP	DTP	DTP	DTP	DTP ^c (DTaP at 15+ months)			DTP or DTaP	Td	
<i>Haemophilus influenzae</i> type b (Hib) ^d		Hib		Hib	Hib ^d		Hib ^d				
Polio, live oral (OPV) ^e		OPV ^e	OPV	OPV	OPV				OPV		
Measles, mumps, rubella (MMR) ^f							MMR		MMR ^f or MMR ^f		
Varicella-zoster virus vaccine (Var) ^g							Var			Var ^g	

Recommended Childhood Immunization Schedule, United States—1996 (continued)

This schedule has been approved by the Advisory Committee on Immunization Practices, the American Academy of Pediatrics and the American Academy of Family Physicians. Vaccines are listed under the routinely recommended ages. Clear bars indicate range of acceptable ages for vaccination. Shaded bars indicate catch-up vaccination: at 11–12 years of age, hepatitis B vaccine should be administered to children not previously vaccinated, and varicella-zoster virus vaccine should be administered to children not previously vaccinated who lack a reliable history of chickenpox.

^a*Infants born to hepatitis B surface antigen (HBsAg)-negative mothers* should receive 2.5 µg of Recombivax HB or 10 µg of Engerix-B. The second dose should be administered at least 1 month after the first dose. *Infants born to HBsAg-positive mothers* should receive 0.5 mL hepatitis B immunoglobulin (HBIG) within 12 hours of birth, and either 5 µg of Recombivax HB or 10 µg of Engerix-B at a separate site. The second dose is recommended at 1 to 2 months of age and the third dose at 6 months of age. *Infants born to mothers whose HBsAg status is unknown* should receive either 5 µg of Recombivax HB or 10 µg of Engerix-B within 12 hours of birth. The second dose of vaccine is recommended at 1 month of age and the third dose at 6 months of age.

^b*Adolescents who have not previously received three doses of hepatitis B vaccine should initiate or complete the series at the 11- to 12-year-old visit. The second dose should be administered at least 1 month after the first dose, and the third dose should be administered at least 4 months after the first dose and at least 2 months after the second dose.*

^cDTP-4 may be administered at 12 months of age, if at least 6 months have elapsed since DTP-3. Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) is licensed for the fourth and/or fifth vaccine dose(s) for children aged 15 months or more and may be preferred for these doses in this age group. Tetanus and diphtheria toxoids (Td), adsorbed for adult use, is recommended at 11 to 12 years of age if at least 5 years have elapsed since the last dose of DTP, DTaP or DT.

^dThree Hib conjugate vaccines are licensed for infant use. If PRP-OMP (PedvaxHIB) is administered at 2 and 4 months of age, a dose at 6 months is not required. After completing the primary series, any Hib conjugate vaccine may be used as a booster.

^eOPV is recommended for routine infant vaccination. Inactivated poliovirus vaccine (IPV) is recommended for persons with a congenital or acquired immunodeficiency disease or an altered immune status as a result of disease or immunosuppressive therapy, as well as their household contacts, and is an acceptable alternative for other persons. The primary three-dose series for IPV should be given with a minimum interval of 4 weeks between the first and second doses and 6 months between the second and third doses.

^fThe second dose of MMR vaccine is routinely recommended at 4 to 6 years of age or at 11 to 12 years of age, but may be administered at any visit, provided at least 1 month has elapsed since receipt of the first dose.

^gVar vaccine can be administered to susceptible children any time after 12 months of age. Unvaccinated children who lack a reliable history of chickenpox should be vaccinated at the 11- to 12-year-old visit.

Reprinted from Table 2, American Family Physician 1996;53(5):1651.

Hemoglobin and Iron Indices
Normal Hemoglobin and Hematocrit Values By Age and Sex

Measurement	Normal Value, By Age			Normal Value, by Gender	
	1-3 Days	1 Month to 2 Years	3-12 Years	Male	Female
Hemoglobin (gm/dL)	19.0 ± 2.2	12.0 ± 1.5	12.5 ± 1.5	15.5 ± 2.0	13.5 ± 2.0
Hematocrit (%)	61 ± 7.4	36 ± 4	38 ± 4	46 ± 5	40 ± 5

Values are the mean ± 2 SD from the mean.

Ferritin: Normal Values

Diagnostic units: ng/mL (mg/L)
SI conversion factor = 1
Normal: Adult male 20-300
Adult female 20-120

Ferritin (ng/mL)	Diagnoses to Consider	Actions to Consider
Decreased <20	Iron deficiency Hypothyroidism	1. Evaluate for GI blood loss 2. CBC 3. Dietary history 4. TSH

Hemoglobin and Iron Indices (*continued*)
Normal Hemoglobin and Hematocrit Values By Age and Sex

Ferritin (ng/mL)	Diagnoses to Consider	Actions to Consider
Increased >300	Iron overload Hemochromatosis Transfusion Hemolytic anemia Liver disease Chronic inflammation Malignancies Hyperthyroidism	1. Iron, TIBC 2. CBC 3. ESR 4. T ₄ , T ₃ U, TSH 5. Bilirubin, albumin, AST

GI, gastrointestinal; CBC, complete blood count; TSH, thyroid-stimulating hormone; TIBC, total iron-binding capacity; ESR, erythrocyte sedimentation rate; T₄, thyroxine; T₃U, triiodothyronine uptake; AST, aspartate aminotransferase.
Reprinted from: Table 45.1 and 60.15. In: Rakel RE, ed. Textbook of family practice. 5th ed. Philadelphia: WB Saunders, 1995:1266, 1587.

Cardiac Dysrhythmia Protocols

Basic Life Support

All cases: Two initial breaths, then compressions 80–100 per minute
One rescuer: 15:2 ratio of compressions to ventilations
Two rescuer or Pediatric: 5:1 ratio of compressions to ventilations

V-Fib, Pulseless V-Tach

CPR until defibrillator ready
Defibrillate 200 J
Defibrillate 200–300 J
Defibrillate 360 J
Intubate, i.v.
Epinephrine 1 mg i.v./ET q3–5 minutes
Defibrillate 360 J after each drug dose
Options:
Lidocaine 1.5 mg/kg i.v. q3–5 minutes to max 3 mg/kg
Bretylium 5 mg/kg i.v.
Magnesium 1–2 g i.v.
Procainamide 30 mg/min i.v. to max 17 mg/kg
Bicarbonate 1 meq/kg i.v.

Stable Ventricular Tachycardia

Airway, oxygen, i.v.
Lidocaine 1–1.5 mg/kg i.v.
Lidocaine 0.5–0.75 mg/kg i.v. q5–10 min to total 3 mg/kg
Procainamide 20–30 mg/min to max 17 mg/kg
Bretylium 5–10 mg/kg over 8–10 min
Consider cardioversion

Pulseless Electrical Activity (EMD)

CPR, intubate, i.v.
Consider hypovolemia, hypoxia, cardiac tamponade, tension pneumothorax, hypothermia, massive PE, drug OD, hyperkalemia, acidosis, massive MI
Epinephrine 1 mg i.v./ET q3–5 minutes
Atropine 1 mg i.v. if heart rate <60/min

Asystole

CPR intubate, i.v.
Confirm asystole in >1 lead
Consider hypoxia, hyperkalemia, hypokalemia, preexisting acidosis, drug OD, hypothermia
Consider external pacing
Epinephrine 1 mg i.v./ET q3–5 minutes
Atropine 1 mg i.v./ET, repeat in 3–5 min

Bradycardia (<60), symptomatic

Airway, oxygen, i.v.
Atropine 0.5–1 mg i.v. q3–5 min up to 2 mg total
External pacemaker
Options: Dopamine 5–20 µg/kg/min
Epinephrine 2–10 µg/min
Consider Isoproterenol

**Stable Wide-Complex
Tachycardia**

Airway, oxygen, i.v.

Lidocaine 1–1.5 mg/kg i.v.

Lidocaine 0.5–0.75 mg/kg i.v.

q5–10 min to total 3 mg/kg

Adenosine 6 mg rapid i.v., wait
1–2 min

Adenosine 12 mg rapid i.v.,
wait 1–2 min

Adenosine 12 mg rapid i.v.,
wait 1–2 min

Procainamide 20–30 mg/min i.v. to
max 17 mg/kg

Bretylium 5–10 mg/kg i.v. over 8–10
min

Consider cardioversion

Unstable Tachycardia (>150/min)

Airway, oxygen, i.v.

Consider brief trial of medications

Consider cardioversion sedation

Synchronized cardioversion 100 J

Synchronized cardioversion 200 J

Synchronized cardioversion 300 J

Synchronized cardioversion 360 J

Stable PSVT

Airway oxygen, i.v

Vagal maneuvers

Adenosine 6 mg rapid i.v., wait
1–2.

min

Adenosine 12 mg rapid i.v., wait
1–2 min

Adenosine 12 mg rapid i.v., wait
1–2 min

If narrow complex, consider
verapamil, digoxin, β -blockers, or
diltiazem,

If wide complex, consider lidocaine
or procainamide

Consider cardioversion

Appendix IV

The Mini-Mental Status Exam

	Maximum Score
<i>Orientation</i>	
1. What is the year, season, day, month, date?	5
2. Where are we (state, county, town, hospital, floor)?	5
<i>Registration</i>	
3. Name 3 objects, then have the patient name them. Give 1 point per correct answer, repeat until all 3 are named (record number of tries ____).	3
<i>Attention/calculation</i>	
4. Begin with 100 and serially subtract 7 until stopped. Stop patient after 5 correct responses. or Ask patient to spell "world" backwards.	5
<i>Recall</i>	
5. Ask patient to name the 3 objects named earlier. Give 1 point per correct answer.	3
<i>Language</i>	
6. Have patient identify a pencil (pen) and watch.	2
7. Ask patient to repeat "no ifs, ands, or buts."	1
8. Have patient follow a 3-step command. "Take the paper in your right hand, fold it in half, and put it on the floor."	3
9. Have the patient read this statement and obey it: "Close your eyes."	1
10. Ask patient to write a sentence.	1
11. Have patient copy a design.	1
Total Score ^a	30

^aSignificant cognitive impairment ≤ 23 .

Reprinted from: Table 1-18. The mini-mental status exam. In: Discroll CE, Bope ET, Smith CW Jr, et al. The family practice desk reference. 3rd ed. St. Louis: Mosby Year Book, 1996.



"Tumor Markers"

Substances Commonly Found Elevated in Association With Certain Cancers and Benign Confounding Causes

Substance	Associated Cancers	Confounding Conditions
Tissue Specific Proteins		
Prostate Specific Antigen (PSA)	Adenocarcinoma of the prostate ^a	Nodular prostatic hyperplasia, prostatitis
Immunoglobulin (monoclonal)	Multiple myeloma	Monoclonal gammopathy of unknown significance
CA 125	Epithelial ovarian neoplasms	Menstruation, pregnancy, peritonitis, endometriosis
CA 19-9	Adenocarcinoma of the pancreas or colon	Pancreatitis, normal individuals (6%), ulcerative colitis
CA 15-3	Breast carcinoma	
Oncofetal Antigens		
Alpha-Fetoprotein (AFP)	Hepatocellular carcinoma Gonadal germ cell tumors ^a (especially endodermal sinus tumor) Yolk sac tumors	Cirrhosis, toxic liver injury, hepatitis
Carcinoembryonic Antigen (CEA)	Adenocarcinomas of colon, pancreas, stomach, lung, breast, ovary	Pancreatitis, inflammatory bowel disease, hepatitis, cirrhosis, tobacco abuse
Hormones		
B-hCG	Non-seminatous testicular cancers ^a Ca lung, breast, ovary Choriocarcinomas ^a	Pregnancy gestational trophoblastic disease
Calcitonin	Medullary carcinoma of the thyroid	Hypercalcemia

^aSerum assays used for diagnosis and management. Otherwise studies of these levels are not for diagnostic purposes, but for follow-up after establishing baseline.

Joseph C. Linscott, D.O. The Ohio State University Family Practice Residency, 1996.

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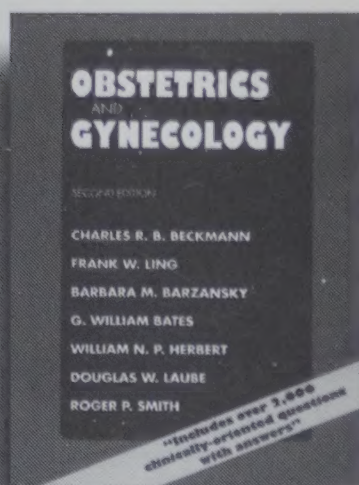
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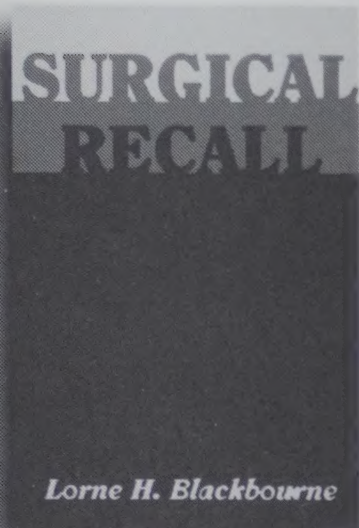
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